FACULTY OF PSYCHOLOGY
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Early sensory attention and pupil size in cognitive control: An EEG approach

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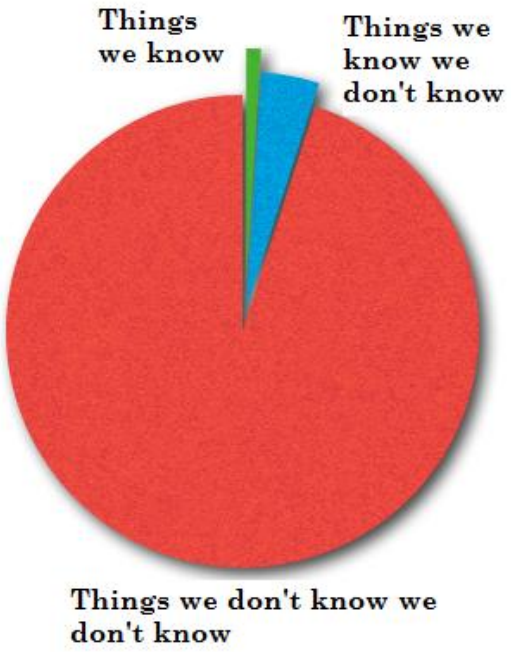
I think that most researchers in the world will agree with this little pie chart, especially those doing brain research. In fact, the red area is probably even larger in reality. Nevertheless, being able to do scientific research is a wonderful thing and I am very grateful that I got the opportunity to do it. Therefore, I'd like to start this dissertation with thanking some people.



First of all, I'd like to thank my promoter **Nico** for being an excellent supervisor and a really nice person to work with on a daily basis. Nico, I admire your profound knowledge of all things related to neuroscience and experimental research and the fact that you just want to do decent research in good conscience (which is not self-evident in

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This is getting long, but please hang on, I'm almost there.

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CHAPTER 1:
INTRODUCTION

"The brain is more than an assemblage of autonomous modules, each crucial for a specific mental function. Every one of these functionally specialized areas must interact with dozens or hundreds of others, their total integration creating something like a vastly complicated orchestra with thousands of instruments, an orchestra that conducts itself, with an ever-changing score and repertoire"

Oliver Sacks

As human beings, we usually do not think about the utter complexity of the most trivial things we do in daily life. We take it for granted that we will wake up when the alarm goes off, we are not surprised that we manage to simultaneously eat breakfast, read the newspaper and check our emails, and find it normal that we are able to navigate our way through rush hour traffic. As cognitive neuroscientists, we do think about all these 'simple' skills and put a lot of time and effort into studying them. Cognitive neuroscience therefore deals with the underlying mechanisms of higher-order cognition and tries to understand how exactly these mechanisms are brought about, how they are based on and influenced by more basic processes like the processing of sensory events that furthermore interact with internal drives, needs, and goals in bringing about behavior. As such, the field of cognitive neuroscience can be situated somewhere between neurobiology and neurophysiology on the hand and neuropsychology and cognitive

psychology on the other hand. Besides analyzing behavioral performance in cognition-related tasks, the most common methodologies to study neural mechanisms are fMRI, EEG/ERP and TMS.

In this dissertation, we present research on early sensory attention and pupil size in cognitive control. Because each chapter has its own introduction and we did not want to repeat ourselves too often, we mainly tried to sketch the bigger picture in this general introduction, defining concepts (*in italics*) and presenting classic theoretical frameworks. First, we will discuss the most prominent findings and models in the field of attention and cognitive control. Additionally, we will focus on adaptations in cognitive control and the interaction between cognitive control and the reward system. Next, we will focus on a well-known indirect marker of attentional processing, arousal and mental effort, namely pupil size. We will discuss the role of pupil size in basic vision and set the stage for one of the main research questions in this dissertation: what is the effect of pupil size on early sensory processes? This will lead us to discuss initial sensory processing in visual cortex, more specifically the primary visual cortex (V1) and its electrophysiological counterpart, the C1. We will end this general introduction with an outline of the different chapters in this dissertation.

ATTENTION

One of the oldest and most fundamental questions in cognitive neuroscience has been related to how humans deal with the overload of information that is picked up by their senses. For example, when you

are reading this dissertation right now, you have to focus on the book in your hands while ignoring almost everything in your surroundings. From pop-up windows on your computer screen to your office mate talking on the phone, you will have to allocate all your attentional resources to the book and block out all other stimuli. Thus far, it could be argued that we just need some kind of general sensory filter. However, things become interesting when the same office mate suddenly mentions your name during his conversation and you look up. Phenomena like this so-called "*cocktail party effect*" led to the development of attention models, which differed with respect to when exactly attentional selection occurred. The *filter model* of Donald Broadbent (Broadbent, 1958) suggested the existence of a filter mechanism deciding which incoming sensory signals could proceed to the next processing stage. Unfortunately, this model could not deal with the aforementioned attentional pop-up of words of semantic importance and was soon replaced by *later selection* models, who argued that all stimuli are non-selectively processed (e.g. Deutsch & Deutsch, 1963). However, late selection models could not deal with the limited attentional capacity and were soon replaced by the seminal *attenuation model* of Anne Treisman (Treisman, 1964). This model proposed attenuation of irrelevant stimuli as the main mechanism of attention, in which stimuli associated with arousal (by semantic meaning or intensity) would have a lower threshold to reach consciousness and further processing than non-arousing stimuli. Furthermore, Kahneman (1973) suggested that the level of arousal and the amount of mental effort required in a specific context determines how much attentional capacity there is to process a stimulus. Ten years and many different

models later, Treisman and Gelade (1980) proposed their *feature integration theory*, in which they also accounted for the complexity of stimuli in a visual search context. Basically, stimuli that are unique from all other stimuli in one discriminative feature would be processed pre-attentively and 'pop-out' (*feature search*), whereas stimuli that can only be identified as a combination of features would need to be searched for by serial processing (*conjunction search*), increasing the search time linearly with the number of distractor items.

It goes beyond the scope of this introduction to review all attention models (for a review, see Pashler, 1999), but it is important to note that attention researchers did not only theorize about *when* attentional selection occurs, but also about *how* it exactly operates. Here, a distinction can be made between *spatial attention* on the one hand and *feature- or object-based attention* on the other hand (for a comparison, see Soto & Blanco, 2004). The first, spatial attention, assumes that attention is directed to a specific location in the visual field. Already in the 19th century, William James (1890) suggested that attention operates as a *spotlight*, with a central focus, a fringe and a margin. Stimuli falling into the central focus are processed with high-resolution, whereas stimuli falling into the fringe are processed with low-resolution. The margin would reflect the outer border of the attentional spotlight, meaning that everything outside of it would not be processed. According to this model, the spotlight has to move across space to process other parts of the visual field (e.g. Posner, 1980). The *zoom-lens* model added the possibility to increase the spatial extent of the attentional focus (Eriksen & St. James, 1986). Assuming a fixed amount of attentional resources, this model predicts slower attentional

processing for large, "zoomed-out", visual areas compared to small areas (Castiello & Umilta, 1992). The second form of attention, feature- or object-based attention assumes that attention is directed to a specific stimulus feature (e.g. color or shape) or object (e.g. lines forming a cubicle), independently from its location in the visual field. Since we often look for a specific object without knowing where it exactly is (e.g. finding your keys on your desk), this is a particularly important form of attention (Theeuwes, 2013).

Unfortunately, using behavioral measurements to study attention has some significant limitations (Luck, Woodman, & Vogel, 2000). First, a reaction time on a single trial is typically measured as the response time to a stimulus. Although this reaction time says something about the duration of the process of interest, it is impossible to know the exact time course of the process. Furthermore, without a response it is even impossible to use reaction time or error rates as dependent variable. Hence, because it can deal with all the problems above, attention researchers have been interested in electroencephalographic (EEG) recordings and the use of event-related potentials since the 1960s (see Box 1 for an introduction to the basics of the EEG and ERP technique). Not only can the continuous ERP waveform be used to directly observe neural activity between a stimulus and a response, it can also provide information about inhibitory processes or the neural suppression of certain stimuli, which is impossible with behavioral measures (Luck et al., 2000).

With respect to spatial attention, it was found that both the *P1* (posterior positivity around 100 ms post-stimulus) and *N1* (posterior negativity around 150-200 ms post-stimulus) have a larger amplitude in

validly cued trials compared to invalidly cued trials in paradigms (Posner, 1980) where stimuli are presented on the left or right side of the screen (Mangun & Hillyard, 1991). Other studies showed that the P1 was primarily smaller for invalid cued trials, whereas the N1 was primarily larger for valid cued trials, indicating that the P1 mainly reflects the suppression of unattended stimuli and the N1 the enhancement of attended stimuli (Luck et al., 1994; see also Slagter, Prinssen, Reteig, & Mazaheri, 2016). Another related distinction is the fact that the P1 primarily reflects whether a target is present or not, whereas the N1 is more related to stimulus discrimination (Vogel & Luck, 2000). When selecting stimuli based on non-spatial features like color and shape (i.e. feature-based attention), the selection negativity (SN) component is often observed (Hillyard & Anllo-Vento, 1998). This component appears between 140 and 180 ms post-stimulus and can have a duration of up to 200 ms. The onset of this waveform indicates when a certain feature is discriminated from the others and attention is solely attributed to it.

Taken together, all these ERP findings support early attentional selection, since differences in attentional allocation to stimuli can be observed as early as 100 ms (and sometimes even earlier; for a review, see Mangun, 2013).

Box 1 - Electroencephalographic recordings and event-related potentials

Electroencephalography (EEG) has been around for a long time. Although the first animal experiments on electrical brain activity date back to the end of the nineteenth century, it was the German physiologist Hans Berger who recorded the first human EEG in 1924. Basically, EEG is a noninvasive technique in which conductive metal electrodes are placed on various locations on the scalp (see Figure 1). When neurons in the cortex are activated, the synaptic excitations of their dendrites produce local current flows that can be picked up by external electrodes as potential differences between a given electrode and a reference site. It is important to note that only large populations of neurons can generate a measurable current flow and that this current flow has to travel through a thick layer of cerebral fluid, skull and skin, which leads to significant attenuation and spatial blurring. Therefore, the EEG signal is only a rough reflection of the underlying brain activity. Conducting electrode gel is injected between the electrode and the skin of the scalp in order to make a connection, and the impedance (which basically reflects the alternating-current counterpart of a resistance) of this connection is lowered as much as possible to increase the signal-to-noise ratio (SNR) and an effort is made to minimize the disturbing influence of electronic devices that send out signals that can be picked up by the scalp electrodes. After amplifying the recorded signal and digitizing the analog signal into a digital one, an online EEG signal can be digitally stored and presented on a computer monitor (e.g. allowing clinicians to monitor epileptic episodes of patients with epilepsy)

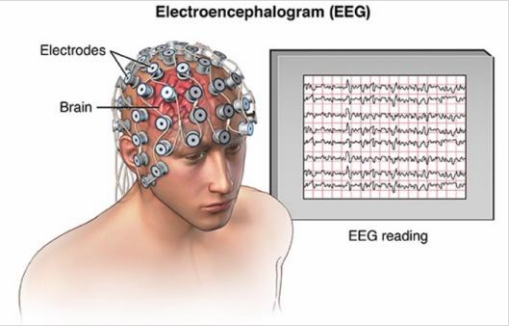


Figure 1. EEG acquisition. Image taken from: https://twitter.com/Psych_Review

In cognitive neuroscience, researchers usually present stimuli or task instructions to participants while recording the EEG signal. Whenever a stimulus is

presented or an event occurs, the computer displaying these stimuli sends a trigger code to the EEG acquisition computer. This allows researchers to time-lock the EEG signal to a certain event and average it over multiple occurrences or replications, leading to event-related potentials or ERPs (see Figure 2). Decades of research have led to a number of important event-related components that can be used as neural markers of certain cognitive processes. Components arising in the first 200 ms after stimulus presentation, like the C1, N1 and P1 are often called sensory/visual evoked potentials because they are related to sensory and attentional processes. Later components like the central N2, N450 or P300 are found to be related to higher-order cognitive processes like conflict processing or oddball detection. All these components are defined by their topographic location, onset latency, duration and polarity, often in comparison to another experimental condition.

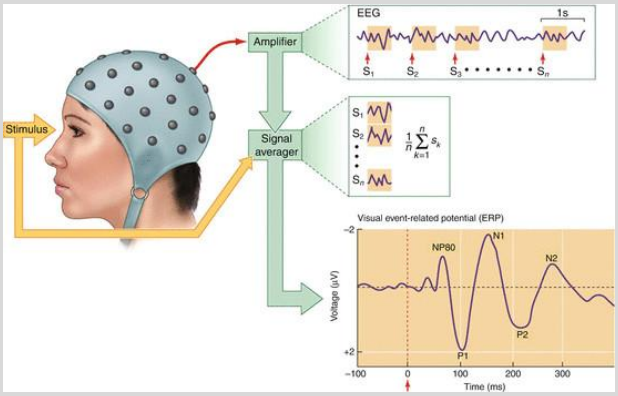


Figure 2. Averaging EEG signals to ERPs. Image taken from Purves et al. (2008)

COGNITIVE CONTROL

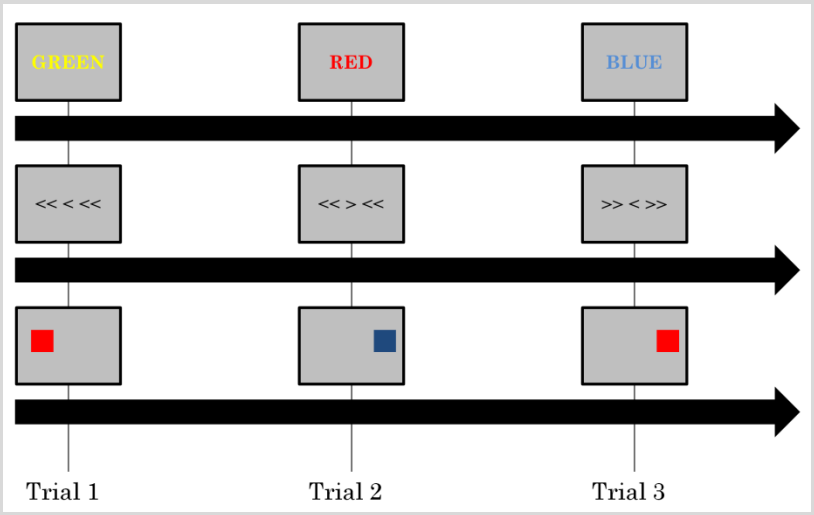
Attention can be considered as one of the most important mechanisms behind the more general *cognitive control* construct and it is even debated if both constructs are separable or not (Cohen, 2017). Nevertheless, cognitive control can be defined as the flexible and adaptive regulation of behavior in the face of conflicting stimuli or responses (Cohen, 2017). For example, when you drive your car and arrive at a crossroad, you have to stop if the traffic light turns red. However, when the driver in front of you ignores the traffic light and drives on, you might be inclined to follow him. Another example would be to stick to your diet and choose for the healthy salad during lunch, although a billboard with a picture of delicious fries seduces you to do otherwise. In these situations, it is often crucial to orchestrate our behavior according to our internal goals or external task demands and to overcome habitual behavior and inhibit prepotent responses. In the following paragraphs, we will first discuss the classical paradigms in cognitive control research and what they exactly measure. Next, we will discuss cognitive control adaptations, with a focus on the conflict adaptation effect. Afterwards, we situate this effect within the dual mechanisms of control (DMC) framework. Finally, we review evidence showing that cognitive control can also be affected when introducing reward incentives.

Cognitive control paradigms

In both the traffic and lunch situation described in the previous paragraph, there was goal-relevant information (the red traffic light and the salad) and goal-irrelevant information (the other driver and the billboard). The presence of both goal-relevant and goal-irrelevant information creates *cognitive conflict* that needs to be overcome in order to reach our goals. In a laboratory context, researchers have developed so-called *congruency tasks* in which participants have to respond to task-relevant information while ignoring task-irrelevant information (Box 2; see Egner, 2008, for different types of conflict). In the Stroop task (Stroop, 1992), for example, participants have to name the ink color of a color word string. Because word reading is the dominant response and overrules color naming, cognitive conflict emerges and participants respond more slowly and less accurately to *incongruent* ('GREEN' printed in yellow) compared to *congruent* ('RED' printed in red) trials. The same goes for the Eriksen flanker task (Eriksen & Eriksen, 1974), in which people have to respond to the direction of the task-relevant target arrow and ignore the task-irrelevant distracter arrows (with usually more distracters than target arrows). In the Simon task, in which people have to respond to the task-relevant shape and ignore the task-irrelevant side of presentation, conflict arises via incompatible activation of the corresponding response hand (Simon, 1969). In all these congruency tasks, the difference in RT or error rates is called the *congruency effect*, which has been used as a marker of effectiveness of cognitive control in thousands of publications by now. The congruency effect can have a different nature depending on the paradigm: there can be conflict because of overlap between the relevant and irrelevant

stimulus dimension (S-S overlap; Stroop and Flanker task) or between the stimulus dimension and the response dimension (S-R overlap: Simon task; for a detailed discussion, see Egner, 2007). Just like early attentional selection, the congruency effect is also reflected in the EEG signal, with specific components like the N450 and N200 signaling cognitive control processes for specific tasks and types of conflict (for an in-depth discussion, see Donohue, Appelbaum, McKay, & Woldorff, 2016; Larson & Clayson, 2011; Larson, Clayson, Kirwan, & Weissman, 2016; Larson, Kaufman, & Perlstein, 2009).

Box 2 - Visual illustration of the most prominent paradigms in cognitive control research. From top to bottom: the Stroop task (respond to font color), the Flanker task (respond to central arrow head) and the Simon task (respond to stimulus color).



The conflict adaptation effect

Seminal cognitive control research has shown that the congruency effect on a given trial could be modulated by the congruency of the

previous trial (Gratton, Coles, & Donchin, 1992). This effect, also known as the *Gratton effect*, the *conflict adaptation effect* or the *congruency sequence effect* (CSE), represents the finding that congruency effects are smaller on trials preceded by incongruent trials compared to trials preceded by congruent trials (for reviews, see Duthoo, Abrahamse, Braem, Boehler, & Notebaert, 2014b; Egner, 2007). In the years following the initial publication of this finding, different theoretical accounts were proposed that mainly differed in their focus on top-down control processes on the one hand and bottom-up associative processes on the other hand (Egner, 2007, 2017).

With respect to top-down control accounts, Gratton himself interpreted his findings as evidence for a strategic effect based on expectations: encountering an incongruent trial would lead to the expectation to encounter another incongruent trial, so participants would strategically enhance their focus on the relevant stimulus information (e.g. ink color or target arrow). The RT and error rate for following incongruent trials would therefore be decreased because of a attenuated influence of distracters, whereas it would be increased for subsequent congruent trials since the benefit of attending congruent irrelevant information would disappear. The opposite is true for expecting congruent trials after encountering a congruent trial: decreased attentional allocation to the relevant information (since it feels redundant) benefits following congruent trials, but increases the RT and error rate of following incongruent trials (Gratton et al., 1992). The seminal *conflict-monitoring model* of Botvinick, Braver, Barch, Carter, and Cohen (2001) explained the CSE along the same lines, but also proposed a computational framework with neuroanatomical

substrates accounting for these mechanisms. They discriminated between two phases of conflict processing: *conflict detection* and *conflict resolution*. When the cognitive control system detects conflict between task-relevant and task-irrelevant stimulus dimensions (through the simultaneous activation of different behavioral response tendencies), it triggers an up-regulation of attentional allocation to the first. From a neuroscientific perspective, the process of conflict detection was mapped onto the dorsal anterior cingulate cortex (dACC), whereas conflict resolution would be associated with activity in the dorsolateral prefrontal cortex (dlPFC). This was supported by many studies showing increased dACC activation during incongruent trials compared to congruent trials (e.g. Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999; Kerns et al., 2004), indicating that the amount of conflict was evaluated in that region. The dlPFC has not only been found to be more active in incongruent trials preceded by incongruent trials, but also to be associated with an increase of attention-related activity in sensory areas (Egner & Hirsch, 2005), reflecting top-down attentional control.

The second category of models accounting for the CSE are usually referred to as associative or bottom-up models (Egner, 2017), because they assume that CSEs arise because of repetitions of stimulus features. The *feature-integration account* of Hommel, Proctor, and Vu (2004) argues that when a task-relevant (e.g. the ink color green) and a task-irrelevant stimulus feature (e.g. the word yellow) are presented with a certain response (e.g. the response button related to the color green), an *episodic memory trace* is created via the process of *binding* (see the aforementioned feature-integration theory of Treisman & Gelade, 1980). Whenever one of the features is presented again on a following trial,

activation is propagated to the other features that were stored together with it, facilitating their attentional processing. This means that when there is a complete repetition or a complete alternation of features, RT and error rate decreases because an episodic memory trace can be retrieved or not (Mayr, Awh, & Laurey, 2003). However, when there is partial repetition in which some features are repeated and others not, the episodic memory trace needs to be overwritten, resulting in an increased RT and error rate (Hommel et al., 2004). It goes beyond the scope of this introduction to discuss follow-up studies adapting cognitive control paradigms in order to discriminate between top-down and bottom-up accounts (for an in-depth discussion, see Duthoo, Abrahamse, Braem, Boehler, & Notebaert, 2014a). However, it is worth mentioning that increasing the number of stimulus features in order to experimentally control for repetitions has led to another possible confound in the CSE (Schmidt & De Houwer, 2011), namely contingency learning. The problem is that more possible combinations of stimulus features lead to relatively more unique incongruent trials compared to congruent trials, while it has been shown that higher-contingent trials (i.e. congruent trials) are responded to faster than low-contingent trials.

Besides pure top-down (Botvinick et al., 2001; Gratton et al., 1992) and bottom-up models (Hommel et al., 2004) explaining the CSE, there is a third category featuring hybrid models combining ideas of the first two (Verguts & Notebaert, 2008, 2009). In a nutshell, models like the *adaptation-by-binding model* of Verguts and Notebaert (2008) proposes that top-down mechanisms trigger an arousal response that binds the current stimulus and response features via Hebbian learning processes.

More specifically, Hebbian learning is increased on incongruent trials compared to congruent trials, making the task-relevant associations stronger. After an incongruent trial, control increases because of this increased connectivity.

Dual mechanisms of control

The dual mechanisms of control or DMC framework proposes two different operating modes of cognitive control: *proactive* and *reactive* control (Braver, 2012; Braver, 2015). Whereas proactive control can be considered as a strategic preparatory mechanism, reflected in preparatory and often sustained activation in control regions like the prefrontal cortex (e.g. Braver, Paxton, Locke, & Barch, 2009; Jimura, Locke, & Braver, 2010), reactive control is a more ad hoc correction mechanism that is triggered by the upcoming stimulus (for an in-depth discussion, see Chiew & Braver, 2017). Applied to our real-life example, proactive control would include preparing your foot to hit the brake when approaching the crossroads or thinking about the nutritional value of a salad before entering the restaurant. Reactive control would be to only move your foot to the brake when the light turns red or to only think about your health when you see the menu card. Unsurprisingly, both operating modes are not mutually exclusive and a great deal of cognitive control research investigates the interaction between the two and how they dynamically adjust control. Interestingly, the DMC framework can also be used to hypothesize about the effects of reward and motivation on cognitive control, which we will discuss in the following paragraphs.

Reward-modulated cognitive control

The goal of resolving cognitive conflict is to adapt our behavior in line with our internal and external goals, which are constantly shaped by motivational factors (Krebs & Woldorff, 2017). You will hit the brake at the right time because your goal is to avoid a car accident with physical or material damage and you will (or at least might) eat the healthy salad instead of the fries because you do not want to gain weight. Motivation can be either *intrinsic* or *extrinsic*, with the first reflecting the desire to accomplish something in order to feel good and the latter reflecting the desire to gain a reward or to avoid a punishment (Ryan & Deci, 2000). In a laboratory context, it is very difficult to study intrinsic motivation because people differ with respect to tasks or behavior they inherently like, and because intrinsic motivation is extremely difficult to modulate in a controlled way (DePasque & Tricomi, 2015). Therefore, cognitive neuroscientists have mainly studied how extrinsic motivation in the form of monetary incentives can modulate cognitive functions like attention and cognitive control (Botvinick & Braver, 2015). Although it is self-evident that the inclusion of reward will lead to repetitions of behavior and/or increased performance (Wise, 2004), it is less clear how this exactly happens in the brain.

With respect to reward modulations in cognitive control paradigms, Krebs and Woldorff recently made a distinction between *pre-task reward cueing* and *stimulus-reward associations* (Krebs & Woldorff, 2017). The first type reflects those situations in which a cue communicates reward availability ahead of the trial for which a response is needed. For example, participants are told that whenever

they see a centrally presented square, they can earn a monetary reward of 10 eurocents if they respond fast and accurate to a subsequent flanker trial. Moreover, this pre-task reward cueing cannot only be implemented on the trial level (transient form), but also on the block level (sustained form). In the latter case, participants are told beforehand that they will earn a monetary reward for fast and accurate responses on each trial in a specific block of trials. The second type, target-reward associations, reflects situations in which one of the stimulus features is related to reward. For example, participants are told that whenever the ink color of a word in a Stroop task is red or yellow, they can earn a monetary reward if they respond fast and accurate (Krebs, Boehler, & Woldorff, 2010).

Obviously, the distinction between pre-task reward cueing and target-reward associations closely resembles the aforementioned distinction between proactive and reactive control. When you prepare to enhance your task performance because of an upcoming reward, a proactive control mechanism seems likely that would optimize attentional allocation. For example, it was found that in a Stroop conflict task rewarded cues led to increased attention for targets, as reflected in a larger CNV (attention-related ERP component) and decreased posterior alpha power (van den Berg, Krebs, Lorist, & Woldorff, 2014). Padmala and Pessoa (Padmala & Pessoa, 2011) also found that reward availability primarily increased performance on incongruent trials in a picture-word interference task, whereas yet another study showed that participants became better at detecting targets in the periphery (Engelmann & Pessoa, 2007). Moreover, the cue-target phase allows for a short time window in which the

underlying neural mechanisms of preparatory, proactive reward processes can be investigated in isolation. The observed activity pattern led to the identification of a *reward system* (including the ventral striatum, the medial midbrain and other dopaminergic areas) that interacts with the brain regions responsible for the task at hand in an experiment (Braver, 2015; Schmidt, Lebreton, Cléry-Melin, Daunizeau, & Pessiglione, 2012).

In contrast, when you cannot predict if an upcoming trial will be rewarded or not, reactive mechanisms will try to reorient attention as soon as possible in case a stimulus feature is associated with reward (e.g. Donohue, Hopf, et al., 2016; Harris et al., 2016). Applied to cognitive control research, Krebs et al. (2010) showed general RT decreases and reduced congruency effects for trials with ink colors associated to reward in a classic four-color Stroop task, showing that reward can modulate conflict resolution in the absence of any global preparatory mechanisms. Follow-up fMRI and EEG experiments showed that this reactive reward processing was most likely based on early visual prioritization of reward-related features (Harris et al., 2016; Krebs, Boehler, Appelbaum, & Woldorff, 2013; Krebs, Boehler, Egner, & Woldorff, 2011). Interestingly, they also observed that when the reward feature (a color in this case) was associated to the task-irrelevant letter string, congruency effects increased. This probably means that the reward feature had a highly distracting effect, even when only conceptually relating to the reward color (i.e. the word meaning rather than font color), making it harder to overcome the stimulus conflict in incongruent trials.

Taken together, cognitive control is a broadly defined concept that

refers to the ability to pursue goal-directed behavior in the face of habitual or prepotent responses. Cognitive control research is closely linked to attention research and an entire research field focusses on control adaptations after experiencing conflict. Finally, motivation and reward are found to be important modulators of cognitive control. In the next section, we will discuss a widely known phenomenon that can also be observed in cognitive control paradigms, as well as during motivational manipulations: pupil size dilation.

COGNITION-RELATED PUPIL DILATION

An interesting finding in the field of cognitive control was that incongruent trials are associated with dilated pupils (Brown et al., 1999; Laeng & Endestad, 2012; Siegle, Ichikawa, & Steinhauer, 2008; Steinhauer, Siegle, Condray, & Pless, 2004). Assuming that the experienced conflict in an incongruent trial leads to an up-regulation of attentional control (Botvinick et al., 2001), the dilated pupil most likely reflects increased mental effort and arousal related to activity in the autonomic nervous system (Siegle et al., 2008).

However, using the pupil as an indirect marker of brain activity is nothing new, since Hess and Pold already showed in 1960 that the pupil not only responds to changes in light (i.e. the *pupillary light reflex*, see Box 3), but also to the emotional value of pictures. In fact, this finding led to an exponential increase in studies reporting pupil size adjustments as a proxy (or indirect marker) of a wide range of cognitive processes (for a review, see Sirois & Brisson, 2014). Most of these cognition-related pupil size changes can be explained by the high

temporal coupling between pupil diameter and activity in the *locus coeruleus-norepinephrine system* (LC-NE system; Costa & Rudebeck, 2016; Joshi, Li, Kalwani, & Gold, 2016). It goes beyond the scope of this general introduction to elaborate on this well-known system (for a review, see Eckstein, Guerra-Carrillo, Miller Singley, & Bunge, 2016), but it is important to note that it is mainly built around the fact that the subcortical *locus coeruleus* (LC) releases *norepinephrine* (NE) throughout the brain (Aston-Jones & Cohen, 2005; Sara, 2009) and that it plays an important role in *attentional state regulation*. For example, according to the seminal adaptive gain theory of Aston-Jones and Cohen (2005), there is an inverted-U relationship between sustained LC activity and optimal performance with respect to attentional allocation. Similar to the classic Yerkes-Dodson arousal curve (Yerkes & Dodson, 1908), high levels of sustained LC activity would be associated with distractibility and an explorative attentional state, whereas low levels of sustained LC activity would be associated with a drowsy and a more exploiting attentional state (Gilzenrat, Nieuwenhuis, Jepma, & Cohen, 2010; Murphy, Robertson, Balsters, & O'Connell R, 2011). In the same way, it was found that task performance would be suboptimal for low and high levels of sustained LC activity, whereas it would be optimal for intermediate levels. Interestingly, the same inverted-U relationship was found between tonic pre-stimulus baseline pupil size and task performance (Gilzenrat et al., 2010; Hayes & Petrov, 2016; Jepma & Nieuwenhuis, 2011; Murphy et al., 2011), making pupil size measurements a useful tool when studying these attentional mechanics.

However, attentional regulation via the LC-NE system is not the only way in which pupil size is modulated. Also emotional arousal

(reflected by increased activity in the autonomic nervous system) can directly modulate the size of the pupil (for a review, see Lang, 2014). Furthermore, it was recently shown that pupil size is also modulated by a top-down mechanism protecting the retina to expected changes in lighting (Ebitz & Moore, 2017; Mathot & Van der Stigchel, 2015). When an ocular movement towards brighter or darker visual object is imminent, our systems already prepares for a pupil change in order not to over- or under stimulate the retinal cells. Taken together, the list of higher-order cognitive processes for which pupil size was measured as a proxy is quite extensive and identifying the nature of the driving mechanism behind cognition-related pupil size changes can sometimes be a challenge (e.g. reward-related processes with both increased mental effort and arousal).

Box 3 - The pupillary light reflex

"Man may either blush or turn pale...but his pupils always dilate."
Irene Loewenfeld, pupillometry pioneer

Visual perception starts with light being reflected off objects in our surroundings and visible light is nothing more than those waves of electromagnetic energy that can be picked up by retinal cells of the human eye. The regulation of the amount of light falling through the pupil onto the retina (i.e. the pupillary light reflex) is controlled by two antagonistic muscles called the sphincter pupillae and the dilator pupillae (see Fig.1), making the pupils respectively constrict in case of brightness (or high levels of light) and dilate in case of darkness (or low levels of light; Diamond, 2001; Eckstein et al., 2016; Loewenfeld & Lowenstein, 1999). These adjustments in pupil size do not just regulate how much light falls onto the retinal cells (affecting "sensitivity" to

light, i.e. the ability to detect dimly lit stimuli in the visual periphery), but thereby also have a direct influence visual acuity (i.e. the ability to see stimuli in detail), yielding a so-called sensitivity-acuity trade-off. When there is a lot of light and the pupil constricts, the image falling on the retina is sharper because the light beams coming from different depths are less refracted and are projected 'correctly' on the retinal plane. This visual acuity is sacrificed when there is little light and the pupil has to dilate to let in enough light to activate the retinal cells, increasing the sensitivity to weak stimuli in peripheral parts of the visual field (Campbell & Green, 1965; Hirata, Yamaji, Sakai, & Usui, 2003; Laughlin, 1992; Loewenfeld & Lowenstein, 1999). The diameter of the pupil can measure between 1.5 and 9 mm, but has an average size of approximately 3 mm under normal lighting conditions (Loewenfeld & Lowenstein, 1999; Sirois & Brisson, 2014).

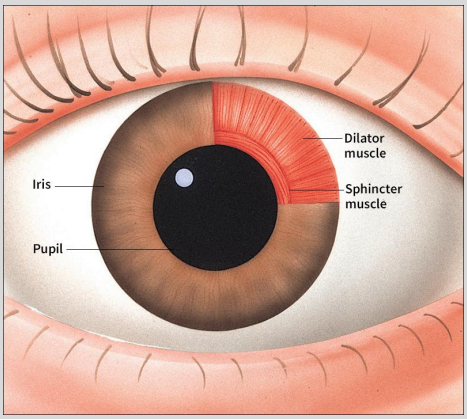


Fig. 1. The sphincter and the dilator muscle controlling the pupil. Image taken from: https://www.thinglink.com/scene/498548908109070337

With respect to cognitive control paradigms, the question arises if the mere change in pupil size also affects the sensory processing of the subsequent trial. Laeng, Orbo, Holmlund, and Miozzo (2011), for example, showed that the maximal difference in pupil size between

congruent and incongruent trials only appeared after 1400 ms and lasted for about 600 ms, making it highly likely that the difference in pupil size still persisted when the next trial was presented. From a wider perspective, this question also relates to the old question on how early in the processing hierarchy attention or higher-order cognition can affect sensory responses (Spence, 1999). In the following section, we will discuss this topic in more detail.

THE FEEDFORWARD RESPONS IN PRIMARY VISUAL CORTEX

When light enters the eye via the pupil and reaches the retinal cells, neural activation is propagated through the optic nerve and subcortical structures to the visual cortex in the occipital lobe, starting at the primary visual cortex (V1), situated at the back of the head (Remington, 2012). Although there are additional pathways circumventing it, primary visual cortex can be considered the first main stage of cortical visual processing, primarily reflecting bottom-up processing of visual input (e.g. Engel et al., 1994; Zhang, Zhaoping, Zhou, & Fang, 2012). Within the visual cortex, an anatomical and functional distinction can be made between the striate visual cortex (primary visual cortex or V1) and the extrastriate visual cortex (V2, V3, V4, V5). Regarding striate visual cortex, research has shown that the visual field is retinotopically mapped, meaning that there is a tight correspondence between a location in the visual field and its location on V1 (Engel et al., 1994; Wandell, 1999; Wandell, Dumoulin, & Brewer, 2007; Wandell & Winawer, 2011). Importantly, light falling onto the fovea of the retina (the area with the highest visual resolution) occupies

more space on V1 than light falling on peripheral parts of the retina ("cortical magnification", see Daniel & Whitteridge, 1961). With respect to its function, V1 has been found to be particularly sensitive to the orientation and spatial frequencies of stimuli and is therefore specialized in edge detection: when a black surface is situated adjacent to a white surface, the dividing line will be encoded in V1 (e.g. Nothdurft, Gallant, & Van Essen, 2000). In extrastriate visual cortex, the complexity of visual processing increases. In V2, for example, cells are not only responsive to orientation, spatial frequency or color, but also to foreground-background discrimination and attention (Roe & Ts'o, 1997). This is reflected by the fact that V2 receives feedforward input from V1 and projects to other extrastriate parts of the visual cortex like V3, V4, MT or V5. It goes beyond the scope of this introduction to discuss all extrastriate subregions (for a review, see Bullier, 2001), but it is important to note that they all have their own specialties like, for example, color coding in V4 (Conway, 2009) and movement detection in V5 (Rokszin et al., 2010), and that this hierarchy is not a one-way street, with feedback loops and recurrent processes playing an active role in its functioning.

Whereas many researchers agree that top-down processes can modulate the extrastriate cortex (Boehler, Schoenfeld, Heinze, & Hopf, 2008; Clark & Hillyard, 1996; Martinez et al., 1999; Noesselt et al., 2002), which is important for the prioritization of visual information in the light of the limited capacity of perception (e.g. Lavie, Hirst, de Fockert, & Viding, 2004), it is still debated if the striate cortex (i.e. V1) can be modulated early on during visual processing. In this context, top-down processes can be understood as attentional or emotional

modulations, broadly referred to as higher cognition. The debate has been mostly studied by means of EEG, with the C1 component (i.e. the first visually evoked potential) as index of V1 processing (Jeffreys & Axford, 1972). This component can be both negative and positive and is normally observed between 50 and 100 ms post-stimulus onset at posterior midline locations (typically measured at electrode POz). In fact, the polarity depends on the presentation location of the stimulus: when a stimulus is presented in the upper visual field (UVF), the C1 will be negative, whereas it will be positive when the stimulus is presented in the lower visual field (LVF; see Box 4). This polarity reversal for upper vs. lower visual field stimulation is explained by the so-called "cruciform model" through a differential mapping of the input to the upper and lower bank of the calcarine sulcus (Jeffreys & Axford, 1972). Methodologically, the C1 component is usually elicited by presenting probe stimuli with a high spatial frequency (for example, a checkerboard pattern or a large number of small horizontal lines) in the periphery of the upper- or lower visual field.

Box 4 - The cruciform model and the C1 component.

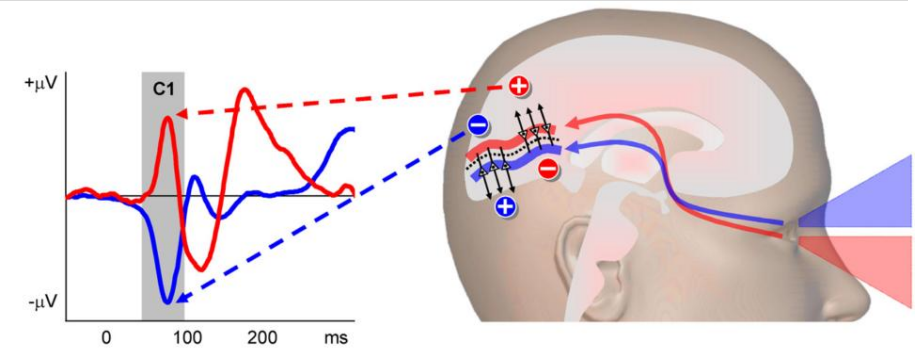


Fig. 1. The polarity reversal of the C1 component. Image taken from K. Rauss, Schwartz, and Pourtois (2011)

On the one hand, there are researchers and research groups arguing that only extrastriate areas like V2, V3, V4 and MT/V5 can be modulated by psychological factors like attention (Clark & Hillyard, 1996; Di Russo, Martinez, & Hillyard, 2003) and not striate areas like V1. Clark and Hillyard (1996), for example, observed attentional enhancements of ERP components that directly follow the C1 (the P1 and N1), but not for the C1 itself. Rather, it has been suggested that V1 activity is only modulated late during visual processing, presumably through delayed feedback signals (Boehler et al., 2008; Martinez et al., 1999; Noesselt et al., 2002). On the other hand, there are also studies showing attentional (Rauss, Pourtois, Vuilleumier, & Schwartz, 2012; Rauss, Pourtois, Vuilleumier, & Schwartz, 2009) or emotional C1 modulations (Pourtois, Grandjean, Sander, & Vuilleumier, 2004; Rossi & Pourtois, 2013; Vanlessen, Rossi, De Raedt, & Pourtois, 2014) .

Importantly, some of these past studies demonstrating C1 modulations did so in task contexts that very likely featured concomitant differences in pupil size. Especially those with a mood manipulation or attentional load manipulation on the block level will have likely showed sustained increased pupil dilation because of effects of emotional arousal and mental effort. Also studies with attentional or emotional manipulations on the trial level, in which the C1-elicting probe was only presented after 400 or 500 ms (i.e. the time the pupil needs to response), might have featured differences in pupil size. However, some of the reported studies did not allow for differences in pupil size (Bayer et al., 2017; Kelly, Gomez-Ramirez, & Foxe, 2008; Pourtois et al., 2004), so it would be inappropriate to argue that pupil

size always acts as a confound in this field of research.

To summarize this section, there is an on-going debate on whether psychological factors like attention and emotion can influence the initial feedforward response in primary visual cortex. One factor that has often been overlooked is pupil size, which might play a role in explaining at least some of the effects.

OUTLINE OF THIS DISSERTATION

Now we have introduced the most important concepts and theoretical frameworks related to early sensory processing, attention, cognitive control and cognition-related pupil dilation and tried to situate the work in this dissertation within the broad field of cognitive neuroscience, it is time to introduce the specific research questions we addressed in the following five chapters.

In **chapter 1,** we focus on the underlying attentional mechanisms of the conflict adaptation effect. As explained earlier in this introduction, cognitive control accounts like the conflict monitoring theory (Botvinick et al., 2001) predict transient, conflict-induced modulations of selective attention, reducing congruency effects on the next trial. Previous research has often used fMRI to study this question, showing modulations in prefrontal structures, motor areas and sensory areas by looking at specialized sensory regions (e.g. Egner & Hirsch, 2005). However, fMRI has a very low temporal resolution, whereas for EEG the possibility exists that the simultaneous enhancement of relevant and suppression of irrelevant information in a cognitive control task might camouflage each other. Therefore, we adopted the paradigm

of Appelbaum, Boehler, Won, Davis, and Woldorff (2012) in which irrelevant information (e.g. the color word) was presented 200 ms before, at the same time or 200 ms after the presentation of the relevant information (e.g. the ink color). The rationale was that this 200 ms time window would allow for an in-depth analysis of "isolated" markers of sensory processing or attention to the relevant or irrelevant stimulus dimension. We started with two experiments using the Stroop task, but ultimately extended our approach also to the Flanker task. Whereas Stroop conflict could involve both spatial and non-spatial attentional operations, Flanker conflict likely mostly relies on spatial attention (Luck & Kappenman, 2012) and previous research had already reported P1 (Scerif, Worden, Davidson, Seiger, & Casey, 2006) and N1 (Suzuki & Shinoda, 2015) modulations in the Flanker task. For each type of conflict task, we had one experiment in which the irrelevant stimulus dimension (word color in the Stroop task or distractor arrows in the Flanker task) was randomly presented before, after, or simultaneous with the relevant stimulus (ink color or target arrow), and one experiment in which the irrelevant information was always presented before the relevant stimulus. This set of experiments developed sequentially based on the fact that we had anticipated finding evidence for attentional adjustments related to conflict adaptation in our first experiment, but failed to do so for most experiments, hence prompting us to run a set of four experiments combining the factors of task (Stroop vs. Flanker) and temporal predictability. We expected that after an incongruent trial less attention would be deployed to the irrelevant stimulus dimension when presented shortly before the relevant dimension, whereas more attention would be deployed in case the

relevant dimension was presented before the irrelevant dimension, since previous fMRI studies found evidence for both mechanisms (Egner & Hirsch, 2005; King, Korb, von Cramon, & Ullsperger, 2010; Polk, Drake, Jonides, Smith, & Smith, 2008).

Although **chapter 2** is not a follow-up on the work in chapter 1 and might seem unrelated at first sight, it was inspired by it nonetheless, and was conducted partly in parallel. As explained earlier on, cognition-related pupil dilation is also observed in conflict tasks (Laeng et al., 2011) and therefore we hypothesized that a dilated pupil on trial *n-1* could still play a role in the processing of trial *n* and hence affect control adjustments like the conflict adaption effect. But in order to study this potential effect in a more systematic way, we decided to focus on low-level visual processing first and design an experiment to study the effect of pupil size on the initial feedforward response without the involvement of higher-order cognition. As far as we know, the rather basic question whether pupil size could have an effect on feedforward V1 activity or not has never been addressed before. Methodologically, we experimentally manipulated pupil size using validated procedures that do not involve differences in luminance or other basic sensory confounds. Specifically, in a first experiment, we used the aforementioned procedure of Binda, Pereverzeva, and Murray (2013) in which participants have to covertly attend either a black or white disk (i.e. central fixation), which has been shown to dilate and constrict the pupils. In a second experiment, we used visual illusions of perceived brightness in order to evoke pupil dilation and constriction (Laeng & Endestad, 2012). In both experiments, we presented a typical C1-eliciting probe (Rossi & Pourtois, 2012) after some delay to allow for the

pupil to change size. Previewing the findings we will present further on in this dissertation, we found that pupil size can indeed directly affect the initial feedforward response in human primary visual cortex (V1), as reflected by a decreased C1 response.

In **chapter 3,** we tried to replicate this effect and to distinguish it further from possible alternative explanations related to the attentional manipulation (attending a dark or bright stimulus in the lateral periphery) that triggered the pupil-size change. We did this by making use of the slow response characteristic of the pupil by presenting a C1-eliciting probe stimulus at a time point that briefly preceded the pupil response (T1) and a time point that followed it (T2). In addition, we report EEG alpha-power lateralization as an index for attentional lateralization in order to demonstrate that the effect we found was driven by mere pupil size and not by alternative explanations like differential attentional deployment.

Chapter 4 returns to the cognitive control topic and describes another combined EEG/eyetracking study in which we report an experiment on sustained or proactive reward effects and their interaction with pupil dilation and attention-related ERP components. As previously mentioned, sustained reward effects have been found to increase task performance and enhance control-related brain activity, in particular in prefrontal cortex in various task domains (e.g. Jimura et al., 2010). In this study, we wanted to extend these findings of sustained effects of rewarded contexts to conflict processing in a typical cognitive-control task like the Eriksen Flanker task. This had been done before in an fMRI context in which a context of potential gain was compared with

a context of potential loss (Paschke et al., 2015), but just like in chapter 1, we wanted to take advantage of the high temporal resolution of EEG and discriminate between the relevant and irrelevant stimulus dimensions (Appelbaum et al., 2012). Participants performed a four-choice Flanker task in which they received monetary rewards for fast and accurate performance in half of the blocks (i.e. rewarded blocks or rewarded context). We hypothesized that in a reward-related context, less attention would be allocated to the distracter arrows, reflected by a decreased attention-related N1 component time-locked to the distracter. In contrast, we expected a larger N1 time-locked to the target arrow in the reward context, as far as this could be measured given the overlap of the preceding distracter processing. With respect to pupil dilation, we expected that a rewarded context should be associated with a sustained increase in pupil dilation, reflected in baseline pupil size. Another hypothesis was that the difference in pupil size between rewarded and non-rewarded blocks could be a marker of the amount of mental effort or attentional allocation, predicting the success of attentional inhibition and potentially the size of the N1 component.

Chapter 5 is the only non-empirical chapter in this dissertation and can be both considered a review and opinion paper. In this chapter, we first give an overview of how higher-order cognitive processes like attention, control and emotion have an effect on the size of the pupil. Next, we refer to some studies showing effects of mere pupil dilation on perceptual processes (including our own work described in chapter 2 and 5) and try to make the point that pupil dilation can play a direct and possibly functional role in human cognition. We do this by also incorporating studies from the field of optics and ophthalmology and

argue that the aforementioned sensitive-acuity trade-off might play a larger role than previously appreciated.

In the final chapter of this dissertation, the **General Discussion**, we will give a brief overview of the results and try to relate them to each other. Moreover, we will try to situate the findings within the existing literature and provide some inspiration for future research.

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CHAPTER 2:

THE ROLE OF TEMPORAL PREDICTABILITY FOR EARLY ATTENTIONAL ADJUSTMENTS AFTER CONFLICT[1]

A frequently-studied phenomenon in cognitive control research is conflict adaptation, or the finding that congruency effects are smaller after incongruent trials. Prominent accounts suggest that this adaptation effect can be explained by transient conflict-induced modulations of selective attention, reducing congruency effects on the next trial. In the present study, we investigated these possible attentional modulations in four experiments using the Stroop and Flanker tasks, dissociating possible enhancements of task-relevant information from suppression of task-irrelevant information by varying when this information was presented. In two experiments, the irrelevant stimulus information was randomly presented shortly before, at the same time, or briefly after the presentation of the relevant dimension. In the other two, irrelevant information was always presented first, making this aspect fully predictable. Despite the central role that attentional adjustments play in theoretical accounts of conflict adaption, we only found evidence for such processes in one of the four experiments. Specifically, we found a modulation of the attention-related posterior N1 event-related potential component that was consistent with paying less attention to the irrelevant information after incongruent trials. This was accompanied by increased inter-trial mid-frontal theta power and a theta-power conflict adaptation effect. We interpret these results as evidence for an adaptive mechanism based on relative attentional inhibition. Importantly, this mechanism only clearly seems to be implemented in a very specific context of high temporal predictability, and only in the Flanker task.

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[1] Bombeke, K., Langford, Z. D., Notebaert, W., & Boehler, C. N. (2017). The role of temporal predictability for early attentional adjustments after conflict. PlosOne, 12(4).

INTRODUCTION

Cognitive control involves the ability to detect conflicting cues in the environment and to adjust our information processing system in order to optimize behavioral responses. These control adjustments invoked by conflict have sparked a lot of scientific interest (for a review, see Duthoo, Abrahamse, Braem, Boehler, & Notebaert, 2014b; Egner, 2007). The "Gratton effect", or conflict adaptation effect, is the hallmark of such research, describing the phenomenon that conflict effects are attenuated after incongruent trials (Gratton, Coles, & Donchin, 1992). Despite alternative accounts (Hommel, Proctor, & Vu, 2004; Mayr, Awh, & Laurey, 2003), the traditionally most accepted explanation for this effect comes from the model of Botvinick and colleagues (Botvinick, Braver, Barch, Carter, & Cohen, 2001), explaining it through a monitoring operation wherein the detection of conflict triggers a transient increase in selective attention, reducing the amount of conflict experienced in the next trial (Botvinick et al., 2001; Kerns et al., 2004; Notebaert & Verguts, 2006; Ullsperger, Bylsma, & Botvinick, 2005). Although there has been an abundance of studies investigating psychological or pathology-related modulations of conflict adaptation effects (Clawson, Clayson, South, & Larson, 2011; Larson, Forrer, & Clayson, 2011), some procedural aspects remain unclear, especially regarding the role of sensory modulations as they unfold rapidly in time. Previous research on this question has predominantly used fMRI, revealing modulations in prefrontal control structures (Kerns et al., 2004; MacDonald, Cohen, Stenger, & Carter, 2000), which trigger subsequent reductions in motor readiness (Danielmeier, Eichele, Forstmann, Tittgemeyer, & Ullsperger, 2011; King, Korb, von Cramon, & Ullsperger, 2010; Marco-Pallares, Camara, Munte, & Rodriguez-

Fornells, 2008) and/or modulations of sensory processing (Danielmeier et al., 2011; Egner & Hirsch, 2005; King et al., 2010). When investigating the role of sensory adjustments, anatomical distinctions between specialized sensory processing modules (e.g. faces, Danielmeier et al., 2011; Egner & Hirsch, 2005; King et al., 2010; Marco-Pallares et al., 2008; Polk, Drake, Jonides, Smith, & Smith, 2008) are usually used. Some of these studies have related this adaptation effect to enhanced processing of the relevant stimulus dimension on n+1 trials (Egner & Hirsch, 2005), whereas others also found inhibition of irrelevant stimuli (Polk et al., 2008).

However, fMRI studies are limited by their temporal resolution and EEG studies have not addressed this question to the same extent. Among the few studies to date, Scerif et al. (Scerif, Worden, Davidson, Seiger, & Casey, 2006) showed a selective enhancement of the visual P1 component for incongruent trials when preceded by incongruent trials in a flanker task with simultaneously presented distractor and target arrows. Interestingly, for no-target flanker trials following incongruent trials, they observed a smaller P1 component. Assuming that conflict detection leads to increased suppression of flanker arrows, this smaller P1 component could be explained as more focused spatial attention. Later, Suzuki and Shinoda (Suzuki & Shinoda, 2015) observed decreased N1 amplitudes for Flanker trials preceded by incongruent stimuli compared to trials preceded by congruent stimuli. This decrease in attentional allocation was correlated with a larger increase in frontal alpha activity, most likely related to proactive frontal control mechanisms. Taken together, these two studies seem to be in line with attentional adjustments after conflict. Yet, these are the only two human EEG studies we are aware of that explicitly look at attentional mechanisms in a sequential conflict-adaptation context, which is

surprising given their theoretical prominence. Moreover, their results differ on the level of which ERP component is affected, and only one of them tried to tap into the specificity of enhancement of relevant vs. suppression of irrelevant information.

A possible pitfall when studying post-conflict adjustments is the possibility of simultaneous enhancement of relevant and suppression of irrelevant information, which might camouflage each other in the scalp EEG using standard paradigms not optimized for such distinctions. Here, we further investigate the nature of attentional modulations during conflict adaptation in a serial reaction time context with a paradigm that has generally been shown to index attentional allocation separately to the relevant and irrelevant stimulus dimension of a conflicting stimulus. The present paradigm was derived from a study employing Stroop stimuli wherein the word and the color component were presented with different stimulus-onset asynchronies (SOAs), varying between -200 ms (word first) to +200 ms (color first) (Appelbaum, Boehler, Won, Davis, & Woldorff, 2012). This study compared blocks where this temporal arrangement was constant versus random, which revealed dissociations for behavioral and EEG markers of conflict. More importantly for the present work, the comparison of the EEG data for the -200 ms condition between these blocks also yielded evidence for an attentional modulation that preceded the presentation of the relevant stimulus dimension, yielding a smaller negativity in the constant-SOA blocks starting approximately 150 ms after the onset of this stimulus dimension. This modulation, due to timing and spatial distribution, was related to a selection negativity (SN; Hillyard & Anllo-Vento, 1998) and was thus interpreted as indexing the degree to which attention was deployed to the word component. Importantly, these data suggest that with temporal predictability, participants are better at

activating temporary selective filters in line with temporal orienting ideas (e.g. Nobre, 2001).

In the present study, we hypothesized that a similar posterior modulation could also be present as a neural marker of attentional adjustments in the conflict adaptation effect in conditions with temporal predictability (i.e., when the irrelevant information was systematically presented before the relevant information). This prediction fits with recent proactive accounts of conflict adaptation. Duthoo et al. (Duthoo, Abrahamse, Braem, & Notebaert, 2014) for instance demonstrated that participants' predictions about the upcoming (in)congruency influence conflict adaptation. However, Jiménez and Méndez (Jimenez & Mendez, 2013, 2014) came to a different conclusion, finding that conflict adaptation mostly depends on the average of experienced conflict in previous trials and not on the participants' expectancies.

Taken together our goals of studying neural attentional markers of conflict adaptation that can be both driven by reactive and proactive control processes, we conducted four experiments with different groups of participants. Based on Appelbaum et al. (Appelbaum et al., 2012), we started with two experiments using the Stroop task, but ultimately extended our approach also to the Flanker task, given the study of Scerif et al. (Scerif et al., 2006) and Suzuki and Shinoda (Suzuki & Shinoda, 2015) with a P1 and N1 modulation in the Flanker task, respectively. For each type of conflict task, we had one experiment in which the irrelevant stimulus dimension (word color in the Stroop task or distractor arrows in the Flanker task) was randomly presented before, after, or simultaneous with the relevant stimulus (ink color or target arrow), and one experiment in which the irrelevant information was always presented before the relevant stimulus. This set of experiments developed sequentially based on the fact that we had

anticipated finding evidence for attentional adjustments related to conflict adaptation in our first experiment, but failed to do so for most experiments, hence prompting us to run a set of four experiments combining the factors of task (Stroop vs. Flanker) and temporal predictability. Furthermore, we planned to explore the context of possible attentional modulations by looking at oscillatory activity before and after the second trial in a conflict adaption sequence, in order to relate to earlier work showing oscillatory power modulations between the two trials (Carp & Compton, 2009; Compton, Arnstein, Freedman, Dainer-Best, & Liss, 2011; Compton, Huber, Levinson, & Zheutlin, 2012; Marco-Pallares et al., 2008) and conflict-related frontal modulations in consecutive trials (Clayson & Larson, 2011a, 2011b; Larson, Clayson, & Baldwin, 2012; Larson, Kaufman, & Perlstein, 2009).

METHOD

Given the similarities between the four experiments with respect to design, acquisition and analysis, the sections below describe common aspects while explicitly pointing out differences.

Participants

For each experiment, participants (experiment 1: n = 23, 9 ♂, 14 ♀; experiment 2: n = 23, 10 ♂, 13 ♀; experiment 3: n = 22, 8 ♂, 14 ♀; experiment 4: n = 22, 10 ♂, 12 ♀, ranging between 18-26 years) were selected on the basis of a prescreening questionnaire via the Experimetrix scheduling system (https://experimetrix2.com/rug/). In these questionnaires, people only had to indicate their age, gender,

handedness and if they had abnormal vision or any neurological disorders. Every interested candidate below 30 years old without abnormal vision (corrected vision was allowed) and neurological disorders would be invited to subscribe for the experiment via the scheduling system. Before completing the experiment, participants signed an informed consent in which they were informed about their right to stop the experiment whenever they wanted. The procedures were approved by the ethical committee of the Faculty of Psychology and Educational Sciences of Ghent University and participants received 25€ for a session that lasted two hours.

Stimuli

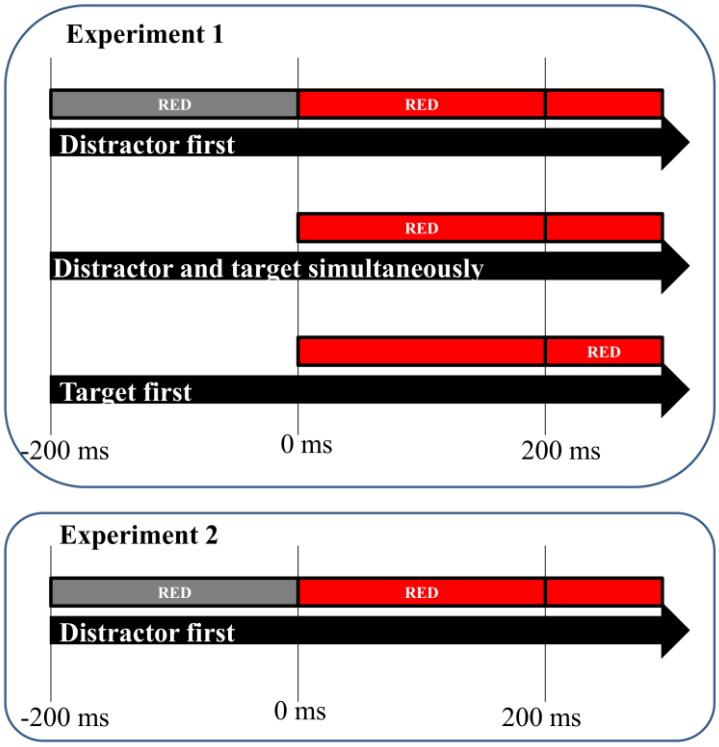
In experiment 1 and 2, the paradigm was based on Appelbaum et al. (Appelbaum et al., 2012). In their variant of the Stroop task, red-, green-, blue- and yellow-colored rectangular boxes overlaid with the color-words "RED","GREEN","BLUE" or "YELLOW" were presented on a gray background with a small fixation dot at the center of the screen. The first independent variable was congruency, so trials could be either congruent (e.g., RED on a red box) or incongruent (e.g., RED on a blue box). In each block, half of the trials were congruent (four different pairings) and half of the trials were incongruent (twelve possible pairings, distributed evenly). The second independent variable was the SOA between the relevant and irrelevant information. In experiment 1, irrelevant information was presented either 200 ms before, at the same or 200 ms after the presentation of the relevant information ("unpredictable timing"). In experiment 2, irrelevant word information was always presented 200 ms before the relevant color information ("predictable timing"). Experiments 3 and 4 used a variant of the Flanker task with arrows pointing in four different directions (left up,

left down, right up, right down). White arrows were presented on a gray background with a small fixation dot at the center of the screen. Other than that, everything was exactly the same as in experiment 1 and 2, respectively, with experiment 3 using the temporal arrangement of experiment 1 and experiment 4 that of experiment 2.

Procedure and design

In experiment 1 and 2 (the Stroop experiments), participants were instructed to manually indicate the ink color of the rectangular box as fast and accurate as possible, while in experiment 3 and 4 (the Flanker experiments) they were instructed to respond to the direction of the target arrow (Fig 1). In the experiments with predictable timing, participants knew that the irrelevant word or distracting arrows would be presented first, while they could not foresee this in the experiments with unpredictable timing. They had to respond by manually pressing one of four keys on the keyboard corresponding to four possible colors or four different arrow directions and they had some time to memorize this response mapping before the start of the experimental phase. Responses were registered until 1300 ms after stimulus onset and there was a jittered inter-trial interval ranging from 900 to 1200 ms. Participants completed 16 pseudo-randomized blocks of 72 trials in experiment 1 and 3 and 10 blocks with the same number of trials in experiment 2 and 4. Every two blocks, participant could take a break. Since we were interested in sequential effects, we chose to have a completely randomized sequence of trials. As a consequence, the proportion of congruent trials preceded by congruent trials (CC), incongruent trials preceded by congruent trials (CI), congruent trials preceded by incongruent trials (IC) and incongruent trials preceded by incongruent trials (II) was always 25%, resulting in 288 trials per cell in experiment

1 and 3 (irrelevant-first, simultaneous and relevant first trials) and 180 trials per cell in experiment 2 and 4 (only irrelevant-first trials).



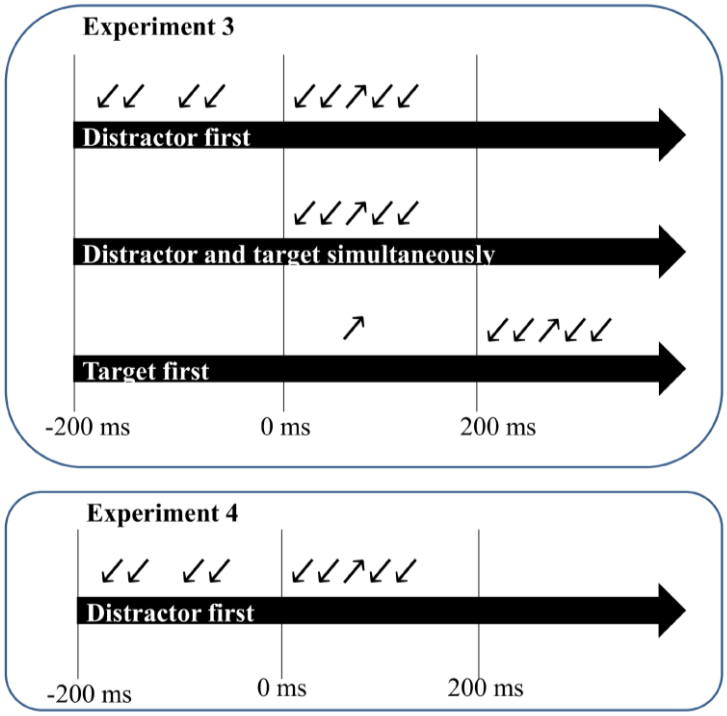


Fig 1. Design of the four experiments. In the Stroop experiments (experiments 1 and 2), participants were instructed to manually indicate the ink color of the rectangular box as fast and accurate as possible, while in the Flanker experiments (experiments 3 and 4) they were instructed to respond to the direction of the target arrow. In the experiments with unpredictable design, irrelevant information could be presented 200 ms before, 200 ms after or simultaneous with the relevant information, while the experiments with predictable design, irrelevant information was always presented first (again by 200 ms).

Behavioral data acquisition and analysis

For RT analyses, the first trial of each block and incorrect or missed responses on trial n and n-1 were excluded and an outlier rejection criterion of 2 SDs was applied. RT and error rates were analyzed with repeated-measures ANOVAs (rANOVAs), with factors

SOA (3 levels), previous congruency (2 levels) and current congruency (2 levels) in experiment 1 and 3, and factors previous and current congruency (each 2 levels) in experiment 2 and 4. In case of significant interactions in experiment 1 and 3, additional rANOVAs and paired samples t-tests were performed on the conflict adaptation effect (i.e. the interaction between previous and current congruency) per SOA condition. The significance threshold was set to a p-value of .05 and, when applicable, adjusted using the Greenhouse–Geisser correction for non-sphericity. Additional outlier removal procedures and/or participant exclusions are described per experiment.

EEG acquisition, preprocessing and analysis

The EEG was acquired with a Biosemi ActiveTwo measurement system (BioSemi, Amsterdam, Netherlands), using 64 Ag-AgCl scalp electrodes attached to a standard international 10-20 system cap. Six additional external electrodes were attached to the head: left and right mastoids, which were used for later offline re-referencing, a bilateral electro-oculogram (EOG) pair next to the outer canti of the eyes to measure horizontal eye-movements and two electrodes above and below the left eye to measure vertical eye movements. Signals were amplified and digitized with a sampling rate of 512 Hz. Next, EEG data was processed using EEGLAB (Delorme & Makeig, 2004) and the ERPLAB plugin (Lopez-Calderon & Luck, 2014), both MATLAB-based. We used a bandpass filter of 0.01-30 Hz on the continuous EEG data. Epochs were always time-locked to the onset of the information that came first, depending on the condition (irrelevant distractors in irrelevant-first condition, both the irrelevant distractors and relevant target in the simultaneous condition and the relevant target in the relevant-first condition). Just like in the behavioral analyses, only trials with accurate

performance on trial N-1 and N were included. Epochs included a 200 ms pre-stimulus period that was used for baseline correction and lasted 1000 ms. Trials with drifts larger than -/+ 200 μV were rejected, leading to a rejection of 5% of the epochs on average. Next, epochs were averaged within and subsequently across participants.

To test for evidence for differential attentional processing of the stimuli between post-congruent and post-incongruent trials and the interaction with different SOA conditions in experiment 1 and 3, we probed for task differences in the -200 ms window in the relevant-first, simultaneous and irrelevant-first condition (time-locked to the onset of the relevant target). The first and third condition provided an uninterrupted window for 200 ms, during which no other overlapping stimulus response activity would be present. Based on previous research on attentional selection (Hillyard & Anllo-Vento, 1998) and the study of Appelbaum et al. (Appelbaum et al., 2012), we probed the response amplitudes over ROIs comprised of left posterior sensors PO3, P3 and P1, and right posterior sensors PO4, P4 and P2. Since all stimuli were presented centrally, we did not expect lateralized effects and hence decided to collapse across the left and right posterior ROI for plotting and analyses purposes. Time windows for measurement were based on Appelbaum et al. (Appelbaum et al., 2012) and visual inspection of the averaged ERP.

In order to probe for theta power modulations, we also performed event-related spectral perturbation analyses. Epoched data (from -500 to 2500 ms) was transformed to the frequency domain using EEGLAB's "newtimef" function (Delorme & Makeig, 2004) and baseline correction was performed using the 500 ms window before the onset of trial n-1 for inter-trial analyses and the 500 ms window before trial n for the current trial analyses. Fifty frequencies between 1 and 30 Hz were sampled

uniformly between -250 and 2250 ms, with 200 sample points in between. We considered 4-8 Hz as the theta range and used the average across the different frequencies for all statistical analyses. In order to measure preparatory activity in the inter-trial interval, we took the interval between 500 and 1000 ms after the response as measurement window. By doing so, we measured oscillatory activity in the 500 ms window before the onset of the next trial (taking temporal jitter into account). Based on visual inspection of the average response across conditions and its temporal proximity to the onset of the response, we chose the 500-600 ms window after stimulus onset in trial n for the measurement of the theta power conflict adaptation effect.

Amplitudes, latencies and power measurements were statistically compared using repeated-measures ANOVAs in experiment 1 and 3 and paired samples t-tests in experiment 2 and 4. For selected analyses, we also reported Bayes factor in order to indicate how likely the absence of an effect was. Current congruency was not included in the analysis, because all measured activity in the window from 0 to 200 ms could only be related to previous congruency (the congruency status of the current trial was not yet determined, since the other dimension only appeared after 200 ms). At latencies beyond ~250 ms, the processing of the second stimulus would begin and would overlap and distort the ERP activity evoked in response to the first one.

RESULTS

Exp 1 - Stroop task with unpredictable timing

Behavior: reaction time

The main effects of SOA and current congruency were significant, $F(2,44)=64.3$, $p < .001$, $r = .86$ and $F(1, 22) = 221.48$, $p < .001$, $r = .95$, respectively, whereas the main effect of previous congruency was not, $F(1, 22) = .1$, $p > .5$, $r = .06$. As expected, trials in which irrelevant distracter information preceded the relevant target resulted in the fastest response, followed by simultaneous and relevant-first trials and participants responded in general faster to congruent trials than to incongruent trials. There was a significant interaction between SOA and current congruency, $F(2,44)= 69.65$, $p < .001$, $r = .87$, showing that the congruency effect on trial n was largest for trials in which the distracter preceded the target and smallest for trials in which the target preceded the distracter. The interaction between SOA and previous congruency did not reach significance, $F(2, 44) = 1.27$, $p > .2$, $r = .22$. An overall conflict adaptation effect, as reflected in the interaction between previous congruency and current congruency, was not present, $F(1,22)=.68$, $p > .5$, $r = .17$. Importantly, the three-way interaction between SOA, previous congruency and current congruency was only marginally significant, $F(2, 44) = 2.56$, $p = .09$, $r = .32$. Because we were mostly interested in the conflict adaptation effect split out per SOA condition, we looked at the interaction between previous and current congruency per condition. The conflict adaptation effect was significant for trials in which the irrelevant word was presented first, $F(1,22) = 5.40$, $p < .05$, $r = .44$, so the congruency effect was smaller after incongruent trials (99.15 ms) than after congruent trials (113.75 ms). Somewhat surprisingly, for trials where the relevant and irrelevant dimension were presented at the same time, the conflict adaptation effect was not significant, $F(1,22) = .51$, $p > .4$, $r = .15$. Also for the condition in which relevant information was presented first, we could

not find a significant conflict adaptation effect, $F(1,22) = .73$, $p > .4$, $r = .18$ (Fig 2A).

Behavior: error rate

On average, participants made an error in 9.23% of the trials. The main effects of SOA and current condition were significant, $F(2,44)=6.26$, $p = .004$, $r = .47$ and $F(1, 22) = 14.78$, $p = .001$, $r = .63$, respectively, whereas the main effect of previous congruency was not, $F(1, 22) = 1.17$, $p = .29$, $r = .23$. Participants made the most errors in trials where the irrelevant information was presented first (8.65%), compared to trials with simultaneous (7.59%) and relevant first (6.59%) presentation. There was a significant interaction between SOA and current congruency, $F(2,44)= 5.18$, $p = .01$, $r = .44$, showing that the congruency effect on trial n was largest for trials in which the distracter preceded the target and smallest for trials in which the target preceded the distracter, but no interaction between SOA and previous congruency, $F(2, 44) = .03$, $p = .97$, $r = .03$. An overall conflict adaptation effect, as reflected in the interaction between previous congruency and current congruency, was not present, $F(1,22)=.71$, $p = .41$, $r = .18$. Also the three-way interaction between SOA, previous congruency and current congruency did not reach significance, $F(2, 44) = 2.04$, $p = .14$, $r = .29$.

ERPs

A repeated-measures ANOVA with factors previous congruency and current SOA performed over a 50-ms window between 150 and 200 ms post-stimulus onset for the collapsed posterior ROIs revealed no significant main effects for current SOA and previous congruency, $F(2,44)=.26$, $p > .1$, $r = .11$ and $F(1,22) = .58$, $p > .1$, $r = .16$, respectively.

Also the interaction between SOA and previous congruency did not reach significance, $F(2,44) = 1.26$, $p > .1$, $r = .23$. Therefore, we did not look at the isolated effect of previous congruency per SOA condition. However, we did calculate inverse Bayes factors (BF01), allowing us to report the likelihood of the absence of the effect. The inverse Bayes factors for the effect of previous congruency on irrelevant-first (BF01 = 11.82), simultaneous (BF01 = 3.78) and relevant-first trials (BF01 = 4.47) showed 'strong', 'substantial' and 'substantial' evidence for the null hypothesis, respectively (Jeffreys, 1998). As can be seen in Fig 2C, there was a difference in posterior activity between 25 ms and 75 ms between post-congruent and post-incongruent trials for irrelevant-first trials. Since it is highly unlikely that activation differences that early can be related to the time-locked event, we interpret this difference as an artifact in the grand average. Overall, it seems clear that there was no early posterior modulation in trial n related to the congruency of trial n-1.

Exp 2 - Stroop task with predictable timing

Behavior: reaction time

There was no main effect of previous congruency, $F(1,22) = 1.77$, $p = .20$, $r = .27$, but a highly significant main effect of current congruency, $F(1,22) = 236.33$, $p < .001$, $r = .96$ (II trials= 622.17 ms; IC trials = 532.72 ms; CC trials = 516.06 ms; CI trials = 621.72 ms). Also the interaction between previous congruency and current congruency, $F(1,22) = 5.09$, $p = .03$, $r = .42$, was significant, indicating the presence of a behavioral conflict adaptation effect (Fig 2B). The congruency effect was smaller after incongruent trials (89 ms) than after congruent trials (105 ms).

Behavior: error rate

On average, participants made an error in 11.24 % of the trials. We both found a main effect of previous congruency and current congruency, $F(1,22) = 9.07$, $p = .01$, $r = .54$, and $F(1,22) = 4.46$, $p = .05$, $r = .41$, respectively (II trials=13.82%; IC trials = 6.91%; CC trials = 8.52%; CI trials = 15.70%). The interaction between previous congruency and current congruency was not significant, $F(1,22) = .07$, $p = .80$, $r = .05$, indicating the absence of an conflict adaptation effect for the error rates.

ERPs

T-tests performed over the averaged 50 ms window between 150 and 200 ms post-stimulus onset for the collapsed posterior ROIs revealed no significant differences between post-congruent ($M = -.90$, $SD = 3.03$) and post-incongruent trials ($M = -.73$, $SD = 2.89$), $t(22)= -0.88$, $p = .39$. Just like in the unpredictable design, we could not observe a posterior attentional modulation as neural marker of conflict adaptation for any of the conditions (Fig 2D). An inverse Bayes factor of $BF01 = 2$ supported 'anecdotal' evidence in favor of the null hypothesis.

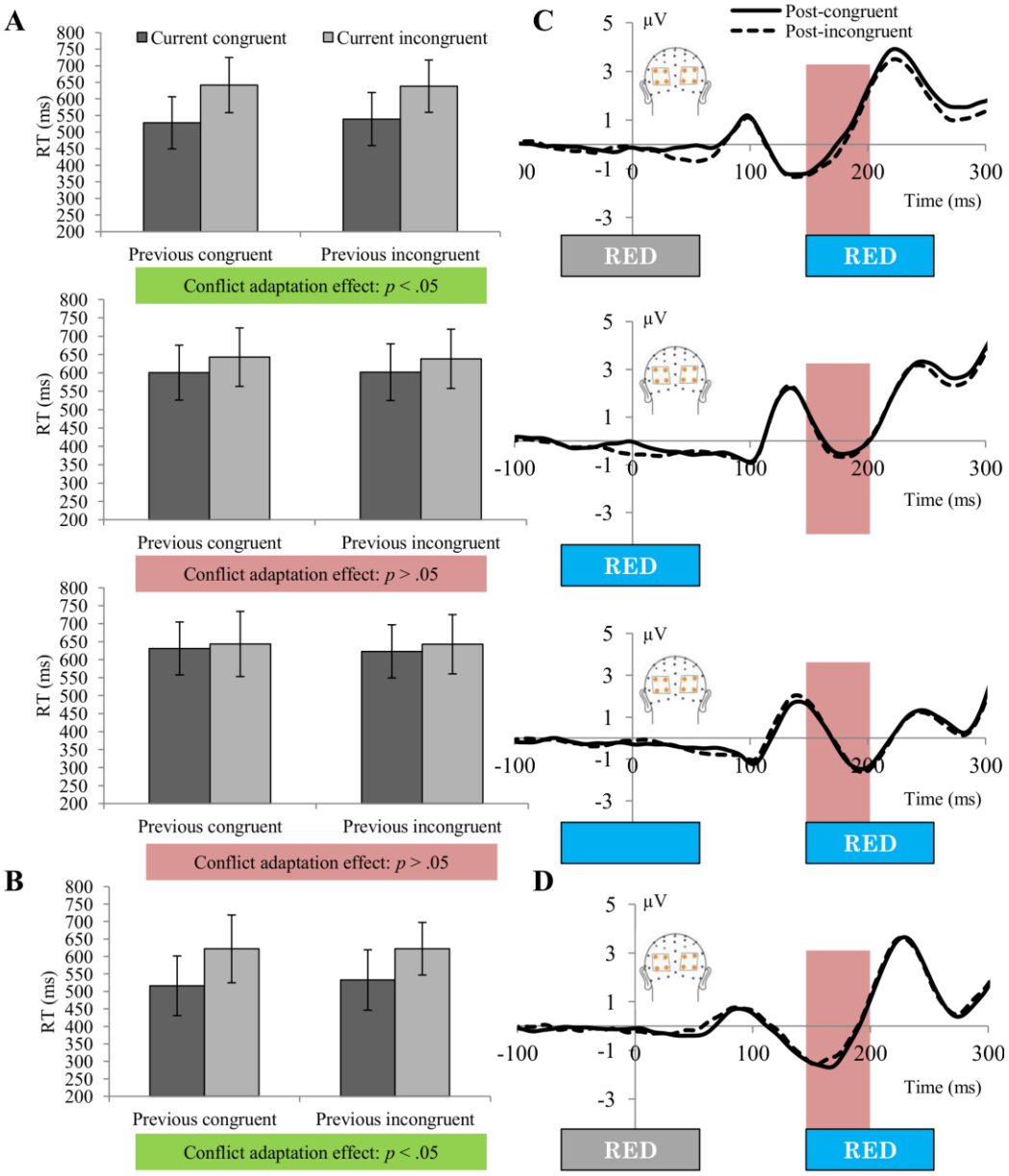


Fig 2. Results of experiment 1&2 - Stroop experiments with predictable and unpredictable timing. (A)(B) Mean reaction times per SOA condition (irrelevant-first, simultaneous and relevant-first in experiment 1, (A); irrelevant-

first in experiment 2, (B)) for current congruent (dark grey) and incongruent (light grey) trials as a function of the congruency level of the previous trial in the Stroop experiments (error bars represent 1 standard deviation around the mean). (C)(D) Early attentional ERP amplitudes (μV) per SOA condition as a function of the congruency level of the previous trial in the Stroop experiments with unpredictable (C) and predictable (D) timing. Measurements were performed for averaged activity over a 50-ms window between 150 and 200 ms post-stimulus onset for the collapsed posterior ROIs, indicated in red (left posterior sensors PO3, P3 and P1, and right posterior sensors PO4, P4 and P2). The irrelevant-first and relevant-first conditions provided an uninterrupted window for 200 ms, during which no other overlapping stimulus response activity would be present. The results show no significant ERP modulations by previous congruency.

Exp 3 - Flanker task with unpredictable timing

Behavior: reaction time

The main effects of SOA and current congruency were significant, $F(1.36,29.91)=134.51$, $p < .001$, $r = .93$ and $F(1, 21) = 554.01$, $p < .001$, $r = .98$, respectively, whereas the main effect of previous congruency was not, $F(1, 21) = .1$, $p > .3$, $r = .20$. Participants responded faster to irrelevant-first trials compared to simultaneous and relevant-first trials. There was a significant interaction between SOA and current congruency, $F(1.49,32.80)= 221.82$, $p < .001$, $r = .95$, showing that the congruency effect on trial n was largest for trials in which the distracter preceded the target and smallest for trials in which the target preceded the distracter. The interaction between SOA and previous congruency did not reach significance, $F(2, 42) = 1.65$, $p > .2$, $r = .26$. An overall conflict adaptation effect, as reflected in the interaction between previous congruency and current congruency, was present, $F(1,21)=.7.85$, $p < .05$, $r = .51$. Importantly, the three-way interaction

between SOA, previous congruency and current congruency was highly significant, $F(1, 42) = 11.23$, $p < .001$, $r = .58$. The conflict adaptation effect was significant for trials in which the irrelevant word was presented first, $F(1,21) = 20.61$, $p < .001$, $r = .7$: the congruency effect was smaller after incongruent trials (86 ms) than after congruent trials (101 ms). For trials where the relevant and irrelevant dimension were presented at the same time, the conflict adaptation effect was not significant, $F(1,21) = 2.50$, $p > .1$, $r = .32$. Also for the condition in which relevant information was presented first, we could not find a significant conflict adaptation effect, $F(1,21) = 1.15$, $p > .2$, $r = .22$ (Fig 3A a).

Behavior: error rate

On average, participants made an error in 5.18% of the trials. The main effects of SOA, current condition and previous condition were significant, $F(2,42)= 25$, $p < .001$, $r = .73$, $F(1, 21) = 40.89$, $p < .001$, $r = .81$ and $F(1,21) = 9.89$, $p = .005$, $r = .56$, respectively. Participants again made the most errors in trials where the irrelevant information was presented first (8.06%), compared to trials with simultaneous (3.84%) and relevant first (3.63%) presentation. There was a significant interaction between SOA and current congruency, $F(1.16,25.4)= 30.43$, $p < .001$, $r = .76$, indicating that the congruency effect on trial n was largest for distracter-first trials, followed by target-first and simultaneous trials. The interaction between SOA and previous congruency did not reach significance, $F(2, 42) = 2.73$, $p = .08$, $r = .33$. An overall conflict adaptation effect, as reflected in the interaction between previous congruency and current congruency, was present, $F(1,21) = 7.66$, $p = .01$, $r = .51$. Also the three-way interaction between SOA, previous congruency and current congruency did reach significance, $F(1.50, 33.02) = 4.16$, $p = .04$, $r = .40$. Splitting out this

conflict adaptation effect for the different SOA conditions resulted in a significant effect for trials in which the irrelevant word was presented first, $F(1,21) = 9.24$, $p = .006$, $r = .54$: the congruency effect was smaller after incongruent trials (10.74% errors) than after congruent trials (15.17% errors). For trials in which the relevant and irrelevant dimension were presented at the same time, the conflict adaptation effect was not significant, $F(1,21) = .21$, $p = .65$, $r = .1$. Also for the condition in which relevant information was presented first, we did not observe a significant conflict adaptation effect, $F(1,21) = .28$, $p = .60$, $r = .11$.

ERPs

A repeated-measures ANOVA with factors previous congruency and current SOA performed over the averaged 50 ms window between 150 and 200 ms post-stimulus onset for the collapsed posterior ROIs revealed a significant main effect for current SOA, but not for previous congruency, $F(2,42)=36.7$, $p < .001$, $r = .80$ and $F(1,21) = .43$, $p > .5$, $r = .14$, respectively. The main effect of current SOA showed the largest ERP response for trials in which the distracter preceded the target, followed by simultaneous and target-first trials. The interaction between SOA and previous congruency did not reach significance, $F(2,42) = .06$, $p > .5$, $r = .05$ (Fig 3C). The inverse Bayes factors for the effect of previous congruency on irrelevant-first ($BF01 = 11.82$), simultaneous ($BF01 = 3.78$) and relevant-first trials ($BF01 = 4.47$) all indicated 'substantial' evidence for the null hypothesis in all three conditions (Jeffreys, 1998). Visual inspection of the stimulus-locked ERP seems to suggest a P1 modulation in the irrelevant-first condition. However, when statistically comparing the average amplitude between

100 and 150 ms in this condition only, a paired samples t-test showed this modulation was not significant, $t(21) = 1.32$, $p > .2$.

Exp 4 - Flanker task with predictable timing

Behavior: reaction time

There was a main effect of previous congruency, $F(1,21) = 15.28$, $p < .001$, $r = .64$ and current congruency, $F(1,21) = 165.55$, $p < .001$, $r = .94$. Also the interaction between previous congruency and current congruency was highly significant, $F(1,21) = 56.234$, $p < .001$, $r = .85$, indicating the presence of a behavioral conflict adaptation effect (Fig 3B). The congruency effect was consistently smaller after incongruent trials (75 ms) than after congruent trials (102 ms)(Fig 3B)

Behavior: error rate

On average, participants made an error in 12.95% of the trials, and there were significant main effects of previous congruency and current congruency, $F(1,21) = 15.93$, $p = .001$, $r = .65$, and $F(1,21) = 20.49$, $p < .001$, $r = .70$, respectively (II trials=18.91%; IC trials = 12.35 %; CC trials = 5.22%; CI trials = 15.30%). Also the interaction between previous congruency and current congruency was significant, $F(1,21) = 5.20$, $p = .03$, $r = .44$, indicating the presence of a conflict adaptation effect for the error rates.

ERPs

A paired samples t-test performed over a 50 ms window between 150 and 200 ms post-stimulus onset for the collapsed posterior ROIs revealed a significant difference between post-congruent (M = -3.09, SD = 2.97) and post-incongruent trials (M = -2.66, SD = 2.89), $t(21)=-3.163$, $p < .01$, indicating a decrease in negative posterior activity after trials with conflict. Based on timing and topography, we interpret this negative-going component as a visual N1 component (Fig 3D). The inverse Bayes factor (BF01 = .05) for the effect of previous congruency in this experiment had a value below 1, providing 'strong' evidence in favor of the alternative hypothesis (i.e. in favor of the modulation).

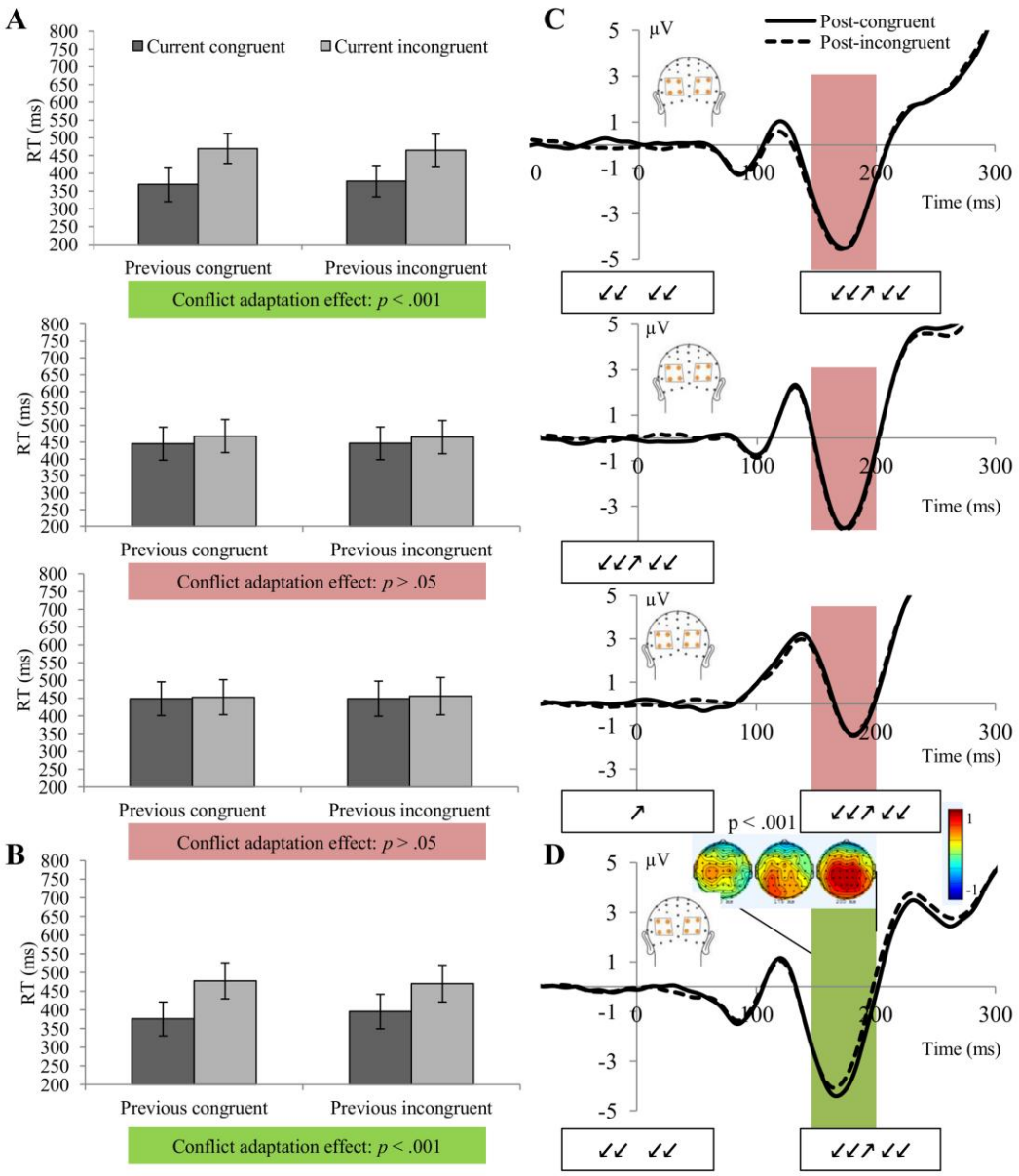


Fig 3. Results of experiment 3&4 - Flanker experiments with predictable and unpredictable timing. (A)(B) Mean reaction times per SOA condition (irrelevant-first, simultaneous and relevant-first in experiment 1, (A); irrelevant-

first in experiment 2, (B)) for current congruent (dark grey) and incongruent (light grey) trials as a function of the congruency level of the previous trial in the Flanker experiments (error bars represent 1 standard deviation around the mean). (C)(D) Early attentional ERP component amplitudes (μV) per SOA condition as a function of the congruency level of the previous trial in the Flanker experiments with unpredictable (C) and predictable (D) timing. Measurements were performed for averaged activity over a 50-ms window between 150 and 200 ms post-stimulus onset for the collapsed posterior ROIs, indicated in red (left posterior sensors PO3, P3 and P1, and right posterior sensors PO4, P4 and P2). The irrelevant-first and relevant-first conditions provided an uninterrupted window for 200 ms, during which no other overlapping stimulus response activity would be present. Only the Flanker task with a predictable irrelevant-first temporal arrangement showed a significant posterior modulation reflecting a decreased negativity starting around 150 ms, likely representing decreased early attentional processing.

Time-frequency decompositions: theta power

Because we found evidence for an attentional involvement in conflict adaptation in the Flanker task with predictable design, we did a time-frequency decomposition on this data to study oscillatory activity preceding and following this attentional modulation, and also provide this data for the random Flanker task for reference. We focused on these two experiments for the sake of simplicity, and because corresponding exploratory analyses for both Stroop experiments did not reveal a consistent result pattern.

Many studies have found that increased oscillatory activity in the theta range (4-8 Hz), measured over fronto-midline scalp electrodes, reflects increased executive functioning during inhibitory processes (Brier et al., 2010; Kirmizi-Alsan et al., 2006; Kovacevic et al., 2012; Tang, Hu, & Chen, 2013). With respect to conflict adaptation, some

researchers found smaller mid-frontal theta power congruency effects after incongruent trials compared to congruent trials (Pastotter, Dreisbach, & Bauml, 2013), whereas others did not (Cohen & Cavanagh, 2011). Moreover, there is some evidence that higher parietal theta power during the inter-trial interval after incongruent trials can be interpreted as proactive adjustments of attentional control (Pastotter et al., 2013). First, we analyzed theta power in the response-stimulus interval after trial N-1, i.e. before conflict adaptation occurs. A two-tailed paired samples t-test performed on mid-frontal theta power measurements over a 500 ms window between 500 and 1000 ms after the response on trial N-1 (measured at Fz) revealed a highly significant difference between post-congruent (M = -0.73, SD = 1.73) and post-incongruent response-stimulus intervals or RSIs (M = .34, SD = 1.32), $t(21)=-2.90$, $p = .008$. On average, theta power increased significantly more after incongruent trials than after congruent trials. Next, we looked at conflict-related theta power in the current trial (Fig 4). A repeated-measures ANOVA with factors previous congruency and current congruency performed over a 100-ms window between 500 and 600 ms after the onset of the irrelevant stimulus information (again measured at FCz) showed a marginally significant main effect of previous congruency, $F(1,21) = 3.90$, $p = .06$, $r = .40$, and a highly significant main effect of current congruency, $F(1,21) = 21.48$, $p < .001$, $r = .72$. Interestingly, there was a significant interaction between previous and current congruency, $F(1,21) = 5.76$, $p = .03$, $r = .47$, showing the presence of a conflict adaptation effect for mid-frontal theta power (CC trials = .43 dB ; CI trials = 2.21 dB; IC trials = .39 dB; II trials = 1.72 dB).

Although we could not identify a neural marker of an attentional contribution to conflict adaptation in the Flanker experiment with an unpredictable design we also probed those data for the above theta effects. For comparability, we only analyzed trials in which the irrelevant information was presented first (just like in the experiment with a predictable design). A two-tailed paired samples t-test performed on mid-frontal theta power in the response-stimulus interval after trial N-1 between 500 and 1000 ms after the response (measured at Fz) showed no significant differences between post-congruent (M = -.89, SD = .93) and post-incongruent RSIs (M = -.97, SD = 1.12), $t(21)=.22$, $p = .83$. With respect to the conflict-related theta power in the current trial, a repeated-measures ANOVA with factors previous congruency and current congruency performed over a 100-ms window between 500 and 600 ms after the onset of the irrelevant stimulus information (measured at FCz) showed no significant main effect of previous congruency, $F(1,21) = .01$, $p = .94$, $r = 0$, but a highly significant main effect of current congruency, $F(1,21) = 24.93$, $p < .001$, $r = .74$ (more theta power for current incongruent trials). There was no significant interaction between previous and current congruency, $F(1,21) = .03$, $p = .87$, $r = .001$, showing the lack of a conflict adaptation effect for mid-frontal theta power (CC trials = .02 dB ; CI trials = 1.85 dB; IC trials = .05 dB; II trials = 1.85 dB).

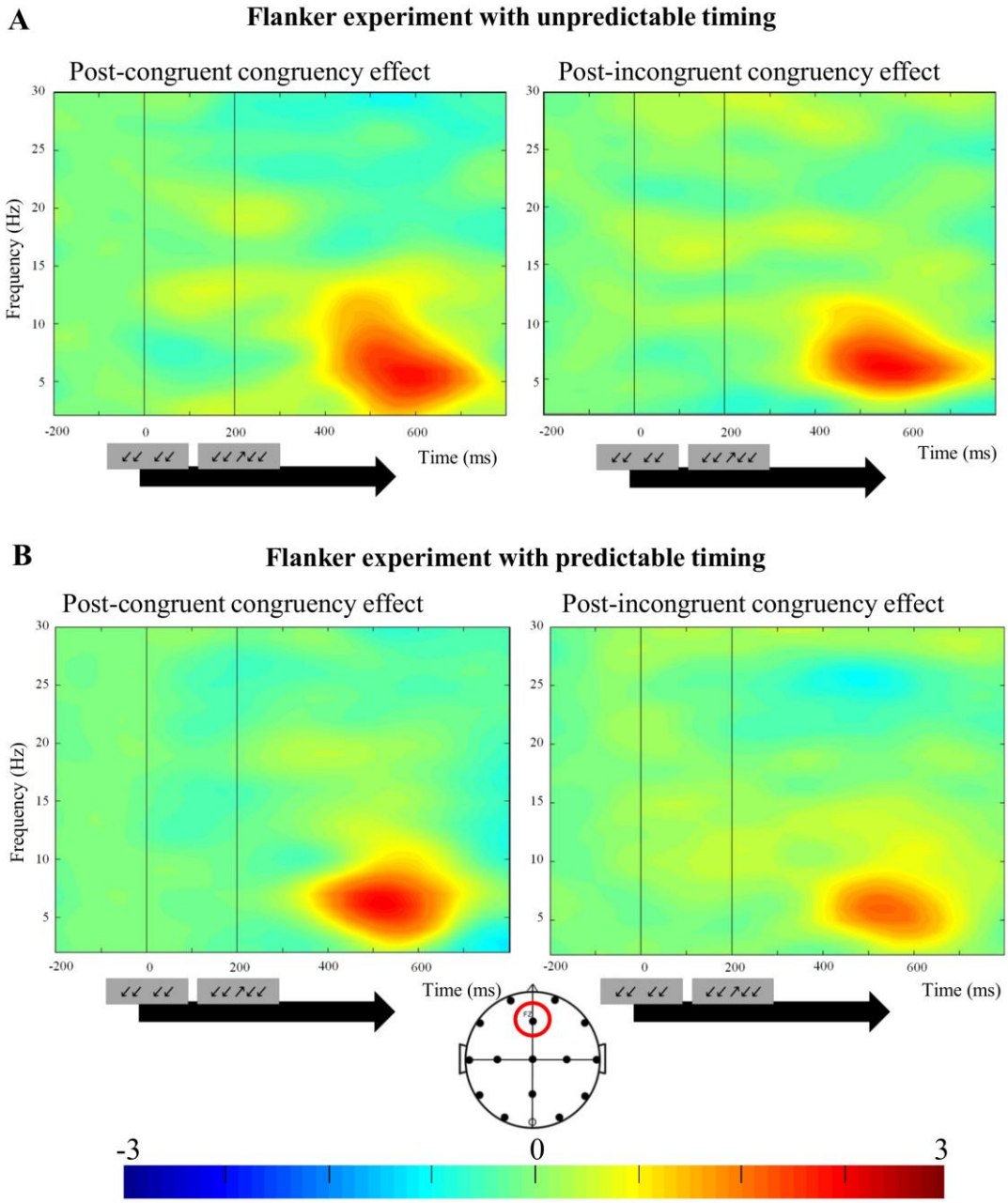

A
Flanker experiment with unpredictable timing
Post-congruent congruency effect
Post-incongruent congruency effect
Frequency (Hz)
Time (ms)
B
Flanker experiment with predictable timing
Post-congruent congruency effect
Post-incongruent congruency effect
Frequency (Hz)
Time (ms)
-3
0
3

Fig 4. Theta power conflict adaptation effect in experiments 3&4 - Flanker experiments with unpredictable and predictable timing. (A)(B) The theta power congruency effect (current incongruent trial minus current congruent trial) in irrelevant-first trials as a function of the congruency level of the previous trial in the Flanker experiments with unpredictable (A) and predictable (B) timing (4-8 Hz as the theta range, measured at Fz). We found evidence for a theta power conflict adaptation effect in the predictable, but not in the unpredictable Flanker experiment.

DISCUSSION

The main objective of this study was to find early attentional EEG markers of conflict adaptation by looking at the effect of previous conflict on early attentional stimulus processing in an optimized paradigm to disentangle specific effects on task-relevant and -irrelevant information processing. Such modulations are generally expected based on theoretical accounts of cognitive control (for a review, see Duthoo, Abrahamse, et al., 2014b; Egner, 2007) , but evidence from techniques with high temporal resolution is scarce. Based on this background, we expected that after an incongruent trial less attention would be deployed to the irrelevant stimulus dimension when presented shortly before the relevant dimension, whereas more attention would be deployed in case the relevant dimension was presented before the irrelevant dimension, since previous fMRI studies found evidence for both mechanisms (Egner & Hirsch, 2005; King et al., 2010; Polk et al., 2008). Yet, we found such modulations only in one out of four experiments, namely in a Flanker task with a predictable irrelevant-first temporal arrangement. More specifically, we observed a posterior modulation reflecting a decreased negativity starting around 150 ms that could be viewed as a decreased visual N1 component based on timing and topography or a (conceptually related) selection negativity (Hillyard & Anllo-Vento, 1998). It is important to note that this modulation took place before the processing of the relevant dimension (i.e. target arrow) began, making it a specific measurement of post-conflict attentional inhibition of irrelevant information. Moreover, this attentional modulation was accompanied by modulations in inter-trial mid-frontal theta power and a theta-power conflict adaptation effect.

Therefore, we interpret these results as evidence for an adaptive mechanism based on relative attentional inhibition.

The fact that we found conflict-adaptation-related attentional modulations in only one of the four experiments was surprising given not just the role they play in theoretical accounts of conflict adaptation but also numerous fMRI findings that are consistent with such an account (Danielmeier et al., 2011; Egner & Hirsch, 2005; King et al., 2010; Marco-Pallares et al., 2008; Polk et al., 2008). Given fMRI's limited temporal resolution, however, data with a higher temporal resolution would be desirable, but the empirical wealth of fMRI work is not equaled in human EEG research, with only two studies explicitly looking at attention in conflict adaptation. Scerif et al. (Scerif et al., 2006) found evidence for a selective enhancement of the visual P1 component for incongruent trials when preceded by incongruent trials in a standard flanker task. More related to this study, when no-target flanker trials were preceded by incongruent trials, they observed a smaller P1 component, which they explained as more focused spatial attention. Similarly, Suzuki and Shinoda (Suzuki & Shinoda, 2015) showed decreased N1 amplitudes for regular Flanker trials after incongruent trials. The crucial difference between these previous studies and our study is our attempt to systematically disentangle modulations of task-relevant and task-irrelevant information by presenting irrelevant information randomly shortly before, at the same time, or briefly after the presentation of the relevant dimension. The fact that we only found the expected modulations in a Flanker task with a predictable irrelevant-dimension-first arrangement might, in part, relate to the fact that it has been suggested that conflict adaptation has a prominent proactive component (i.e., reflecting the expected nature of the n trial, rather than just reactively to that of the n-1 trial). This

would depend on the ability or tendency of predicting the features of the subsequent trial (Duthoo, Abrahamse, et al., 2014b; Duthoo, Abrahamse, Braem, & Notebaert, 2013), which is less possible in experiments with unpredictable timing in the present study. As for the experiments with predictable timing, we limited ourselves to the irrelevant-first condition for the reason that this set-up yields strong conflict adaptation, which relevant- first does not (Appelbaum et al., 2012; Appelbaum, Meyerhoff, & Woldorff, 2009), and still splits out one aspect of stimulus processing, which simultaneous presentations do not. If attentional adjustments occur reactively, we hypothesized that such mechanisms would also be visible in the task variants with unpredictable timing, which, however, we did not observe. Yet, this choice obviously limits our ability to diagnose possible effects of attentional enhancement of relevant information to the random-SOA context, which by itself is rather atypical. Still, our results favor the notion that the attentional modulation we found in a predictable context probably does not occur in a purely reactive way and cannot easily be generalized to other contexts.

Interestingly, we did find a significant behavioral conflict adaptation effect in all four experiments, but only for trials in which the irrelevant flanker distractors or word names were presented 200 ms before the relevant target. The fact that there was a significant conflict adaptation effect in both experiments with predictable distracter-first trials is very much in line with the studies by Weisman and colleagues (Weissman, Egner, Hawks, & Link, 2015; Weissman, Jiang, & Egner, 2014) who also found that conflict adaptation is larger when irrelevant distracter information is always presented before the target information. With respect to the lack of conflict adaptation in relevant-first and simultaneous trials, it is possible that participants simply

ended up experiencing very little cognitive conflict on trial n, leading to an absence of conflict adaptation effects. This would be in line with the findings of Appelbaum and colleagues (Appelbaum et al., 2009), showing much larger congruency effects for trials in which irrelevant information was presented first (but see (Roelofs, 2010) for alternative findings). Therefore, the absence of conflict adaptation on the behavioral level for trials with simultaneous and relevant-first presentation in both Stroop and Flanker experiments seems to reflect a context effect, which abolishes conflict adaptation in a standard condition with simultaneous presentation of relevant and irrelevant stimulus information, likely through a shift from reactive to proactive control processes. However, it is important to note that the behavioral measures of conflict adaptation were of limited interest to this study, since they are also determined by the current congruency status of the trial and do not reflect the processing of irrelevant or relevant information in an isolated way.

A possible explanation why the attentional modulation only occurred in the Flanker task might be related to differences in attentional mechanisms. Specifically, the Flanker task emphasizes spatial attention, whereas the Stroop task would seem to be more related to feature attention (Polk et al., 2008). It might be the case that the modulation we found is only related to spatial filtering of the visual field (after conflict, less attention is allocated to the visual field on the left and right of the target location), which can explain its absence in the Stroop task. If we relate these considerations back to the much more developed area of fMRI evidence for attentional modulations, it is worth noting that a large number of these studies used variants of the Stroop task that present relevant information in the form of categories for which specialized processing modules exist (often faces). It seems possible that such a set-up is more amenable to attentional

modulations, although with fMRI it is impossible to determine their precise timing. Given that the Stroop task is likely more related to feature attention, it is possible that we simply failed to detect this kind of attention because it does not show up easily in the ERP.

When extending our analysis to theta power modulations, we found evidence for a theta power conflict adaptation effect in the predictable, but not in the unpredictable Flanker experiment. Notably, previous research has reported mixed findings on this issue. Pastotter et al. (Pastotter et al., 2013) conducted a response-priming task and did observe a current trial conflict adaptation effect in mid-frontal theta power. Moreover, they found that this theta power adaptation effect correlated with the behavioral conflict adaptation effect. In contrast, Cohen and Cavanagh (Cohen & Cavanagh, 2011) only found a theta power conflict adaptation effect on the single-trial level but failed to find it on the trial-averaged level. It was suggested that this effect might be harder to find in tasks with both stimulus and response conflict like the Stroop and Flanker task than in response-priming task with only response conflict. Nevertheless, we did find the effect and the fact that the theta power evidence for conflict adaptation is only present in the experiment with the attentional modulation supports the notion that it can indeed be a neural marker of the post-conflict adaptation mechanism (i.e. inhibition of irrelevant information) in a predictable context. This raises the possibility that features related to the predictability of stimulus features play a role in whether or not such a neural conflict adaptation pattern is observed or not. Furthermore, we observed increased post-conflict inter-trial theta power, time-locked to the response of trial n-1 in the predictable, but not in the unpredictable Flanker experiment. Pastotter et al. (Pastotter et al., 2013) also observed higher parietal theta power during the inter-trial interval

after incongruent trials, which they interpreted as proactive adjustments of attentional control. Our finding of such a modulation in the task context that also showed an attentional modulation of the attentional processing of the subsequent trial is therefore highly consistent with this notion.

Finally, not controlling for feature integration (Hommel et al., 2004) and contingency learning (Schmidt & De Houwer, 2011) processes in the different experiments is likely a limitation of the present study, as far as disambiguation along such lines goes. The reason why we intentionally did not control for these confounds has to do with the fact that recent accounts of conflict adaptation argue against a strict distinction between feature integration, contingency learning, and other types of cue learning, as learning itself is considered the mechanism behind cognitive control (Abrahamse, Braem, Notebaert, & Verguts, 2016; Egner, 2014). Within this new perspective, it would even be artificial to exclude all learning possibilities and design an experiment where trial n shares no features of trials n-1 (Duthoo, Abrahamse, Braem, Boehler, & Notebaert, 2014a). In other words, when taking away more learning possibilities, we would have reduced conflict adaptation, making it harder to find ERP markers of underlying neural processes. So although it is true the present findings cannot unambiguously discriminate between cognitive control and learning processes, we see those as inherently related, and we do not think this invalidates the conclusions we make on the underlying mechanisms of the conflict adaptation effect.

CONCLUSION

In sum, although we expected to find both a decrease in attentional allocation for irrelevant distractor information and an increase for relevant target information during conflict adaptation, we could only identify the former, and only in a very specific task context of a Flanker task with a temporal arrangement in which the irrelevant stimulus dimension was always presented first. Given this specificity, our experiments emphasize the role of strategic top-down processes.

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CHAPTER 3:

PUPIL SIZE DIRECTLY MODULATES THE FEEDFORWARD RESPONSE IN HUMAN PRIMARY VISUAL CORTEX INDEPENDENTLY OF ATTENTION[1]

Controversy revolves around the question of whether psychological factors like attention and emotion can influence the initial feedforward response in primary visual cortex (V1). Although traditionally, the electrophysiological correlate of this response in humans (the C1 component) has been found to be unaltered by psychological influences, a number of recent studies have described attentional and emotional modulations. Yet, research into psychological effects on the feedforward V1 response has neglected possible direct contributions of concomitant pupil-size modulations, which are known to also occur under various conditions of attentional load and emotional state. Here we tested the hypothesis that such pupil-size differences themselves directly affect the feedforward V1 response. We report data from two complementary experiments, in which we used procedures that modulate pupil size without differences in attentional load or emotion while simultaneously recording pupil-size and EEG data. Our results confirm that pupil size indeed directly influences the feedforward V1 response, showing an inverse relationship between pupil size and early V1 activity. While it is unclear in how far this effect represents a functionally-relevant adaptation, it identifies pupil-size differences as an important modulating factor of the feedforward response of V1 and could hence represent a confounding variable in research investigating the neural influence of psychological factors on early visual processing.

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[1] Bombeke, K., Duthoo, W., Mueller, S., Hopf, J-.M., & Boehler, C. N. (2016). Pupil size directly modulates the feedforward response in human primary visual cortex independently of attention. Neuroimage, 127, 67-73.

INTRODUCTION

A classic question in psychology and neuroscience is how early in the processing hierarchy attention can affect sensory responses (Spence, 1999), a question that is also relevant for related processes like the influence of emotion on sensory processing (Vuilleumier, 2005). In humans, the earliest cortical response to visual stimuli arises in V1 after around 60 ms, which is reflected in the C1 component of the human EEG (Jeffreys and Axford, 1972). Traditionally, it has been found that this component is not amenable to modulations by psychological factors like attention (Clark and Hillyard, 1996; Di Russo et al., 2003). Rather, it has been suggested that V1 activity is only modulated late during visual processing, presumably through delayed feedback signals (Boehler et al., 2008; Martinez et al., 1999; Noesselt et al., 2002). Clark and Hillyard (1996), for example, observed attentional enhancements of ERP components that directly follow the C1 (the P1 and N1), but not for the C1 itself. Contrasting with this view, some recent studies have described attentional (Kelly et al., 2008; Rauss et al., 2012; Rauss et al., 2009) and emotional C1 modulations (Pourtois et al., 2004; Rossi and Pourtois, 2013; Vanlessen et al., 2014; Zhu and Luo, 2012). For example, Rauss et al. (2009) varied attentional load between task blocks in a discrimination task and demonstrated decreased C1 amplitudes for peripheral task-irrelevant stimuli under increased attentional load. Interestingly, often such modulations were limited to the upper visual field (VF), possibly stemming from the lower spatial resolution of the upper VF, which can hence profit more from attentional enhancements (Pourtois et al., 2008; Rauss et al., 2009). Yet, despite these recent observations, the general notion of attentional and

other psychological C1 modulations remains controversial (Ding et al., 2014).

Intriguingly, one possibly important factor has thus far been completely overlooked in this controversy, namely pupil size. Pupil size is known to be modulated by numerous psychological factors, including many of the factors that were recently shown to affect feedforward V1 activity like attentional load and different emotional states (Sirois and Brisson, 2014). This co-occurrence of pupil-size differences with these psychological factors is possibly very relevant since it is conceivable that modulations in V1 activity arise (at least in part) directly from differences in pupil-size rather than from e.g. attentional influences on neural processes in the visual system. Specifically, on a basic level, vision research has shown that pupil size alters the optical properties of the eye (Campbell and Green, 1965), affecting the amount and dispersion of light on the retina and consequently feedforward processing of visual information. This suggests that some of the controversy regarding cognitive-affective differences in early visual processing could depend on the size of the pupil at the moment when the C1 is elicited. In this context it is particularly relevant that in the majority of studies reporting psychological C1 effects, the psychological process of interest is engaged some time before a C1-evoking stimulus is presented, leaving enough time for pupil-size changes to occur, and comparisons are often made between trial types that differ in attentional load or emotional state, or even between different experimental blocks, or different participants (e.g., Rauss et al., 2012; Rauss et al., 2009; Rossi and Pourtois, 2012a; Vanlessen et al., 2014). This overview suggests that it is quite likely that these studies indeed featured different pupil sizes for the different experimental conditions

at the moment when the C1 was elicited. Here, we test whether pupil-size variations can directly affect early feedforward visual processing, as indexed by the C1 component.

To address this question, we simultaneously recorded EEG and pupil-size data of human observers in two complementary experiments that modulated pupil size in a fashion devoid of differences in stimulation luminance, attentional load, emotional state, or effort allocation. In Experiment 1, participants covertly attended to a white or a black disc, which were simultaneously presented in the left and right VF (Figure 1A). Covert attention to these discs modulates pupil size, despite the display being physically identical (Binda et al., 2013; see also Mathot et al., 2013). In Experiment 2 we presented visual illusion stimuli that elicit an illusory brightness perception despite equal overall physical luminance (Figure 2A; Laeng and Endestad, 2012). Importantly, in both experiments, there was enough time for the pupil to dilate or constrict (roughly 2 seconds on average) before presenting the C1-eliciting stimuli in the upper VF or lower VF, as modeled after earlier work investigating the C1 (Rauss et al., 2011). Based on this set-up, we hypothesized that pupil size would affect the amplitude of the C1 despite the fact that pupil size was modulated in a fashion that was devoid of differences in attentional load or related psychological processes.

METHOD

Participants

Twenty-six participants (between 19 and 25 years of age; 8 males, 18 females) participated in one session comprising both experiments. All procedures were approved by the ethics committee of the Faculty of Psychology and Education Sciences of Ghent University. All of them reported perfect vision (no glasses or contact lenses) and no history of psychiatric or neurological disorders. They provided written informed consent and received a monetary compensation of 25 euros. Due to communication failures between the EEG machinery and the eyetracker, the data of one participant in Experiment 1, and that of two participants in Experiment 2, had to be excluded from the analysis.

Procedure and design

Experiment 1

For this experiment, the procedure of Binda et al. (2013) was adopted (Figure 1A). In each trial, three arrows pointing left or right (e.g., <<<) were presented at fixation. After 300 ms, a white and a black disc (11.3° in diameter, centered 10.4° left and right of fixation) were presented against a middle grey background. Depending on the orientation of the arrows, participants had to covertly orient their attention to the white or black disc on a given trial. Participants were told to keep accurate fixation and to minimize blinking. Their gaze was closely monitored based on the online signal of the eyetracker (see Supplementary Material for average fixation durations across the display), which participants were informed about to further reduce their tendency to move their eyes. During disc presentation, task-irrelevant

stimulus arrays (“probes”) with 22 columns of 6 white horizontal lines were presented in the periphery for 200 ms in order to elicit the C1 component (27.6° x 5.1° of visual angle, vertical distance from closest edge to fixation 6.6°). This general set-up was modeled after earlier work investigating the C1 component (Rossi and Pourtois, 2012a). These probes were either presented in the upper VF or in the lower VF. This separation into upper VF and lower VF stimulation is standard for C1 experiments since an important identifying feature of the C1 is its polarity reversal for upper vs. lower VF stimulation, explained through a differential mapping of these inputs to the upper and lower bank of the calcarine sulcus (see the "cruciform model", Jeffreys and Axford, 1972). Direction of attention (attend left or attend right), position of the white and black disc (white left/black right or white right/black left) and probe location (top or bottom) were randomized and fully counterbalanced across trials. With reference to the start of the trial, the C1-eliciting probes were presented either after 1800 ms, 2200 ms, or 2600 ms. These different SOAs were used to de-correlate the and the probe response, as well as to avoid exact predictability for when probes would be presented. Moreover, we included them in order to assess possible differential pupil-size modulations in different time frames, which however turned out to be quite stable across this time range, so that the data was ultimately collapsed across the different SOAs. The white and black discs disappeared 3200 ms after trial onset, followed by a randomly jittered inter-trial interval ranging in duration between 1000 to 1500 ms. Experiment 1 consisted of two blocks of 168 trials, separated by a break. Each block contained 24 (14.3%) rare targets and 144 (85.7%) regular trials. Rare targets were color changes (light blue to yellow, chosen such that the discrimination was similarly difficult in the

black and the white disc) in the center of the disc that participants were covertly attending. For such events, which never occurred in the unattended disc, participants had to press the space bar. This color change could occur before or after the presentation of the C1-eliciting probe, ensuring attentional orienting to the attended disc during the entire duration of the trial. Because rare targets and regular trials were randomly intermixed, participants could not predict target trials.

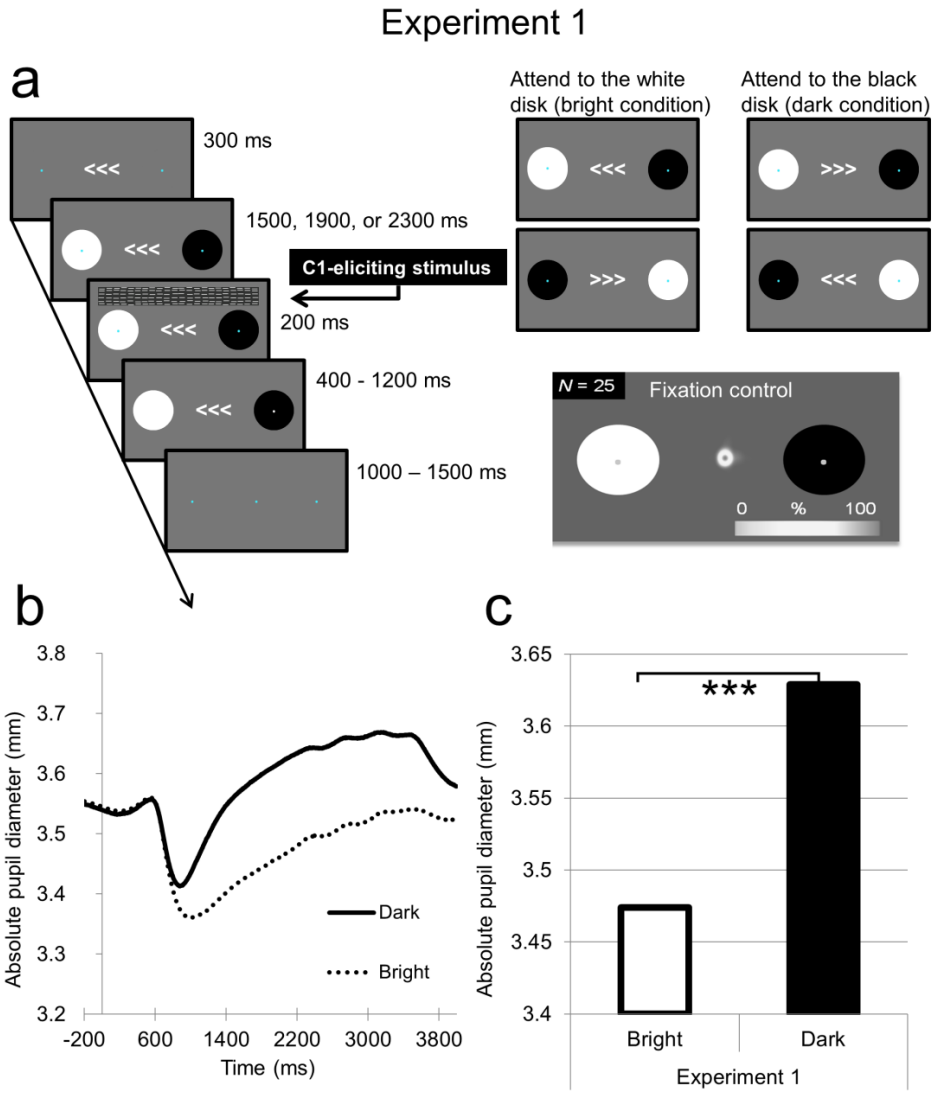

Fig 1. Experiment 1. (A) Trial examples specifying durations of the different events. Note that C1-eliciting stimuli were presented in the upper VF and lower VF in different trials (upper VF in this example). Pupil size was modulated by orienting participants' attention covertly to the white or black disc. (B) Time course of absolute pupil size change. (C) Pupil-size averages

*quantified around the moment of C1 stimulation as used in the statistical analysis (*p < .05, ***p < .001).*

Experiment 2

The second experiment was based on the experimental set-up of Laeng and Endestad (2012), using visual illusion stimuli ("Asahi illusion"; Figure 2A). Observers usually report an impression of brightness when looking at the Asahi illusion on the left in Fig. 2A, in that it is perceived to have a bright center point, while the Asahi illusion on the right is perceived as rather dark in the middle. However, it is important to note that the two illusions only differ in terms of perceived brightness, while their overall physical luminance is constant. In this experiment, participants were asked to fixate a small dot at the center of two possible visual illusions in the absence of any other immediate task. Again, participants were told to keep accurate fixation and to minimize blinking. In order to motivate participants to stay focused and to actively perceive the illusions, they were told they would get a questionnaire about the subjective brightness of the illusions, but otherwise there was no behavioral task. Each trial started with a fixation dot presented for 100 ms, followed by the bright or dark illusion (presented full screen). While fixating the middle of the illusion, C1-eliciting probes with the same number of line segments as in Experiment 1 (24.07° x 4.15° of visual angle, vertical distance from closest edge to fixation 3.69°) were presented for 200 ms in the upper or lower VF, following a variable interval of 1800 ms, 2200 ms or 2600 ms (as in Experiment 1). Again, results were quite stable across these SOAs, leading us to collapse across them again. Note that the spatial arrangement was different from Experiment 1 for configuration

reasons, but that also this experiment was successful in eliciting C1 components for the two hemi-fields. Yet, the probe responses in both experiments are not directly comparable as a consequence of these differences. The illusion remained on screen for 400 ms after probe offset, followed by a randomly jittered inter-trial interval ranging between 1200 to 1500 ms. Visual illusion (bright illusion or dark illusion) and probe location (top or bottom) were again counterbalanced in a randomized fashion across trials. The experiment consisted of three blocks of 112 trials, separated by two self-paced breaks. Each block contained 16 (14.3%) illusion-only trials and 96 (85.7%) regular trials. The only difference between illusion-only and regular trials was the absence of C1-eliciting probes in the former. We included this type of trials as a manipulation check, to obtain a clean estimate of pupil-size effects, which pilot experiments had shown to be less pronounced than the ones in Experiment 1.

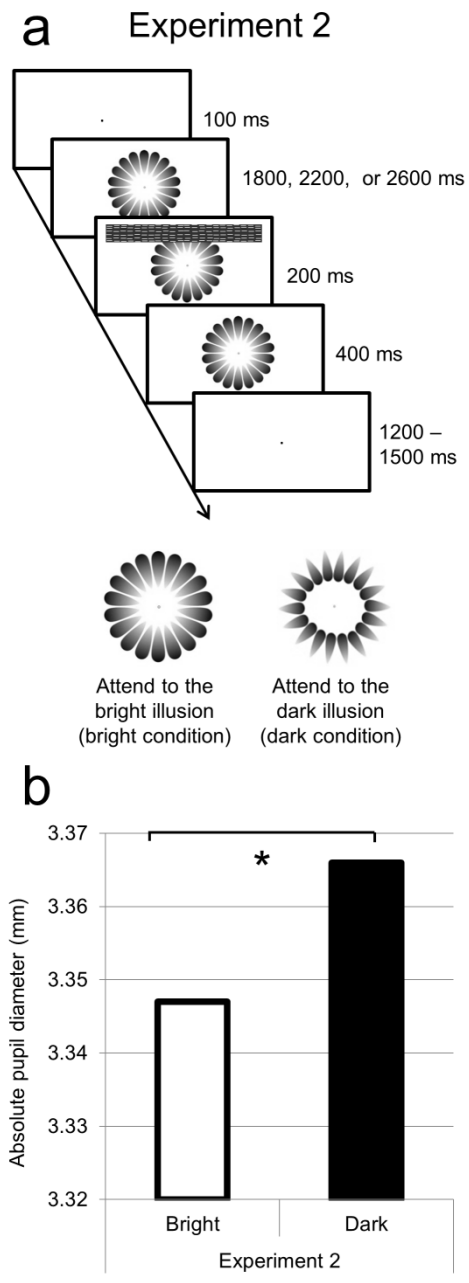

Fig 2. Experiment 2. (A) Trial example specifying durations of the different events. Again, the example shows a trial with C1 stimulation for the upper VF. Below the trial example, iillustrations of the bright and dark illusion

*are shown. (B) Pupil-size averages around the moment of C1 stimulation as used in the statistical analysis (*p < .05, ***p < .001).*

Pupil measurements and preprocessing

A 300 Hz Tobii table-mounted eye tracker (TX300; Tobii Technology AB – www.tobii.com, Danderyd, Sweden) was used to measure pupil size during the experiments. The set-up included a 17-inch computer screen with a built-in camera and infrared LED optics. A chinrest was used to minimize head movements and to maintain a fixed distance of 62 cm from the screen, which is the optimal viewing distance for this type of eyetracker. Each experiment started with a calibration procedure in which participants had to follow a moving red dot to nine locations on a white background. The EEG chamber was dimly lit constantly throughout the experiments. Missing data points due to blinks or recording errors were corrected for by means of a linear interpolation procedure. Trigger codes in both the pupil and EEG data were synchronized. Pupil size was initially recorded at a sampling rate of 300 Hz, but then downsampled to 256 Hz to match the sampling rate of the EEG.

Electrophysiological recordings and preprocessing

EEG data were collected by means of a Biosemi ActiveTwo system (Biosemi, Amsterdam, Netherlands) using 64 Ag-AgCl scalp electrodes positioned according to the standard international 10-20 system. Additional electrodes were attached to the left and right mastoids and electrodes were placed at the outer canthi of both eyes and directly above and below the left eye for acquiring a horizontal and vertical electrooculogram. Signals were recorded with a sampling rate of 256 Hz. During preprocessing, data was re-referenced offline to the average of

the left and right mastoid. Next, a low-pass filter of 30 Hz was applied. Blinks were corrected using independent component analysis (ICA). The data were epoched from -100 ms to 300 ms, time-locked to the onset of the probe stimuli. Automatic artifact rejection was performed on these epochs, removing a small number of trials with extreme values (larger than -/+ 200 μV) or extreme sample-to-sample differences (larger than 150 μV).

Analyses

The absolute pupil diameter in millimeters was used in all analyses, but similar results were obtained with baseline-corrected data (-200 ms pre-stimulus period with reference to disk/illusion onset). Pupil size was measured as the average diameter in the window starting 50 ms before (C1-eliciting) probe onset and ending 50 ms after it. Note that due to the slow dynamics of the pupil response, this time window does not reflect any response to the C1-eliciting probe stimuli yet. Rather the chosen time window captures the pupil size at the moment these probes were presented. The pupil size data were collapsed across the three different SOAs and the two possible probe locations in both experiments. Those values were analyzed using two-tailed paired-samples t-tests to compare pupil size for the respective bright and dark conditions in both experiments.

The C1 component was defined as negative or positive deflections peaking between 70 and 110 ms over occipito-parietal sites (measured at electrode position POz) following probe onset. In order to increase comparability, we chose this measurement window and electrode position based on previous studies showing attentional modulations of the C1 component (Rauss et al., 2012; Rauss et al., 2009; Rossi and

Pourtois, 2012a). EEG data was baseline-corrected using the 100 ms period preceding probe onset. For the statistical analysis, the mean amplitude between 70 and 110 ms was used, but similar results were obtained with peak amplitude measures. Two-tailed paired-samples t-tests were used to compare C1 amplitudes and average pupil sizes between the bright and dark conditions separately for the upper and lower VF, given that C1 modulations have been reported in the upper VF but not the lower VF (Pourtois et al., 2008; Rauss et al., 2009).

RESULTS

Behavior

For experiment 1, the proportion of correct responses for detecting color changes while covertly attending the white or black disc was 0.84 and 0.82 respectively, which did not differ significantly, $t(23)= -.58$, $p > .5$. The reaction time was on average 1575 ms for change detection in white discs and 1590 ms for change detection in black discs, again not yielding a significant difference, $t(23)=.47$, $p > .5$. Both behavioral parameters hence suggest similar task difficulty and mental effort allocation in both conditions. Experiment 2 did not have a task component.

Pupil size

Pupil size was successfully manipulated in both experiments. In Experiment 1, a two-tailed paired-sample t-test comparing average pupil size while attending covertly to the white or black disc was conducted. On average, participants' pupils measured 3.474 mm (SD = 0.402 mm) in diameter at probe onset when covertly attending the white

disc, and 3.629 mm (SD = 0.380 mm) when covertly attending the black disc, $t(24) = 6.65$, $p < .001$ (Figure 1B and Figue 1C). For Experiment 2, participants' average pupil size measured 3.347 mm (SD = 0.321 mm) in diameter at probe onset for the bright illusion, and 3.366 mm (SD = 0.325 mm) for the dark illusion (Figure 2B). While small in amplitude, a two-tailed paired-sample t-test indicated that the difference was significant, $t(23) = -2.23$, $p = .04$. Collectively, these results indicate that both experiments modulated pupil size successfully and in the expected direction.

C1 response

In line with our hypothesis, these pupil-size differences at the moment when the C1 was elicited indeed modulated the amplitude of the C1 response. In Experiment 1, significant occipito-parietal C1s were evoked in both the upper and lower VF (Figure 3A). Given the fact that some earlier studies have often only found C1 modulations for the upper VF, two-tailed paired-sample t-tests were conducted separately to compare the effect of disc color in each VF, using the time-range of interest from earlier studies that have shown attentional C1 modulations (Rossi and Pourtois, 2012a). C1 amplitudes were significantly different for probes in the upper VF (-0.75 μV and -0.10 μV on average for bright and dark discs, respectively), $t(24) = -2.77$, $p = .01$, with larger amplitudes when participants attended the bright disc, but not for probes in the lower VF (2.50 μV and 2.57 μV for bright and dark discs, respectively), $t(24) = -.30$, $p > .5$, which parallels earlier observations that reported C1 modulations exclusively in the upper VF

(Pourtois et al., 2008; Rauss et al., 2009)[2].

In Experiment 2, we again analyzed C1 amplitudes for the upper and lower VF separately. For the upper VF, a two-tailed paired-sample t-test again showed a significant difference between the bright and dark condition (on average -2.37 μV and -1.51 μV for bright and dark illusion, respectively), $t(23) = -3.21$, $p < .01$, but no significant effect for the lower VF (on average 4.52 μV and 4.32 μV for bright and dark illusion, respectively), $t(23) = .68$, $p > .5$ (Figure 3B). Just like in Experiment 1, mean C1 amplitudes for the upper VF were smaller when the pupil was large compared to when the pupil was small. Again, no such relationship was found in the lower VF.

[2] Since the positive overshoot between approximately 90 ms and 110 ms might create the erroneous impression of a 7-fold C1 amplitude modulation, we also compared the C1 component in a more narrowly focused window around the peak (from 60 ms to 90 ms). A two-tailed paired-sample t-test for the C1 elicited in the UVF showed a border-significant difference between the bright and dark condition based on values that might better represent the amplitude relationship between the two conditions (-2.18 μV and -1.53 μV peak amplitudes for bright and dark discs, respectively), $t(24) = -2.04$, $p = .05$.

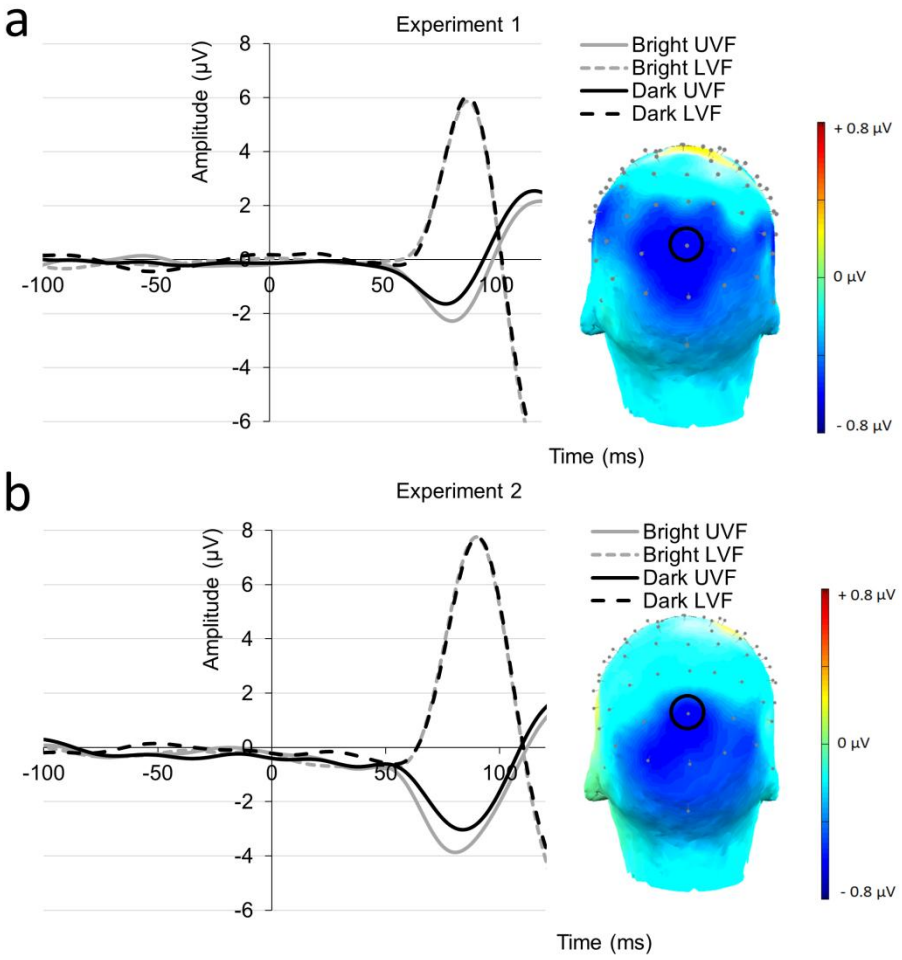

Fig 3. C1 results. Grand-average C1 components (at POz, see black circle in topographical maps) for Experiment 1 (A) and Experiment 2 (B). The topographical distributions show the bright-minus-dark difference in the upper VF condition, averaged between 70 and 110 ms post probe onset. UVF = upper visual field, LVF = lower visual field.

DISCUSSION

Our study addressed the important and unresolved question whether pupil size can influence the initial feedforward response in human V1 (as reflected by the C1 component of the EEG) independently of psychological factors like attentional load and emotion. To this end, we used spatial cuing of covert attention to a dark vs. a bright disk (Experiment 1) and stimuli that elicit illusory differences in brightness perception (Experiment 2) in order to modulate pupil size, which was then followed by task-irrelevant probes in the upper or lower VF eliciting the C1. This orthogonality of our pupil-modulating procedure to psychological factors like attentional load and emotional content was critical in order to demonstrate the pure effect of pupil size on the C1 component.

In line with our hypothesis, we found a significant inverse relationship between pupil size and C1 amplitude in both experiments, albeit only for probe stimuli presented in the upper VF; a visual field specificity that was also found in studies that demonstrated psychological modulations of the C1 (Pourtois et al., 2008; Rauss et al., 2009). The general finding of a relationship between pupil size and C1 amplitude raises the question whether earlier findings of C1 modulations by psychological factors like attentional load or emotional state might not have also, at least in part, reflected pupillary rather than neural mechanisms. This possibility also relates to typical design features in the majority of these earlier studies. As discussed already in the introduction, most of these studies could well have entailed differential pupil size between conditions of interest at the moment when the C1 was elicited. On the one hand, those studies manipulated

psychological factors that are known to affect pupil size, like attentional load, and on the other hand often compared trials from different blocks or even participants. Rauss et al. (2009), for example, implemented a detection task with an experimental design featuring blocks with high attentional load and blocks with low attentional load, finding an attenuated C1 amplitude for the high attentional load blocks. It is quite likely that on average the mean pupil size was higher in the high attentional-load blocks, suggesting that their findings could have at least partially been driven by differences in pupil size. Therefore, it seems generally important that both past and future studies investigating psychological effects on V1 activity are considered in the light of possible contributions from pupil-size differences in different conditions.

A likely explanation for its effects on V1 activity refers to how varying pupil size affects the optical transmission of the eye and its consequences on early cortical processing. Classic work by Campbell and Green (1965) documented an inverse relationship between pupil size and contrast sensitivity. The larger the pupil, the more optical aberrations of light transmission appear, and hence visual resolution decreases. Given V1's sensitivity for sharp edges (e.g., Nothdurft et al., 2000) and the fact that our C1-eliciting probes consisted of horizontal lines with a relatively high spatial frequency and sharp luminance contrasts (as is typical for stimuli designed to elicit a C1), decreased contrast resolution is a very plausible cause for the reduced C1 amplitude in the conditions with larger pupils in our study. Importantly, this relationship between pupil size and contrast sensitivity is only clearly present in the upper VF. It has been shown that at a given spatial frequency, contrast sensitivity is substantially

higher for lower VF stimuli (Skrandies, 1985), which in turn might make the lower VF immune to pupil-related optical effects on the order of magnitude studied here. Nevertheless, in theory, other combinations of exact stimulation parameters and pupil size differences would probably also produce differences in the lower VF. Yet, it is also important to note that the effect of pupil-size on the C1 (in the upper VF) does not seem to scale linearly with the size of the pupil-size modulation. Specifically, the change in pupil size was much more pronounced in Experiment 1 than in Experiment 2, but C1 modulations were quite similar, suggesting a non-linear relationship in which already small size deviations can have a significant effect.

We assume that the mechanism behind the present C1 modulations is directly related to varying pupil size rather than to neural mechanisms. Yet, the pupil-size modulation is still brought about in a fashion that depends on prior neuro-cognitive processes, so that we cannot fully exclude other possible contributions. For example in experiment 1, attention was generally involved in the sense of spatial attention (attending to a white or black disc on the left or on the right); yet, this attentional cuing was spatially orthogonal to the locations of the C1-eliciting stimuli, which were presented in the upper and lower visual field. Therefore, it seems very unlikely that such lateralized attention to a dark or a bright disc would have an effect on the processing of a task-relevant probe stimulus in the upper or lower visual field. Moreover, we made sure that the rare targets present in those discs were equally easy to detect in either disc. Importantly, it has been suggested that the pupil-size adjustment in this task context represents an anticipatory process preparing an eye-movement to a location that differs in brightness from what you are currently looking

at, hence starting a light reflex before the eye is even moved (Mathot and Van der Stigchel, 2015). This suggests a functional role for such pupil-size adjustments that is independent of processes like attentional load and such a mechanism seems very unlikely to globally affect V1 responsiveness on a neural level. In addition, the pupil-size modulation was brought about in a rather different fashion in Experiment 2, where it was based on the mere visual perception of stimuli with different illusory brightness, without even featuring a task component.

Despite all of these considerations, it is theoretically still possible that neural processes, rather than optical ones, have directly contributed to our C1 modulation. Specifically, the mere fact that one is perceiving a stimulus as bright, or attending a bright surface, is likely coded in the visual system (despite overall physical luminance being identical with its respective counter conditions), which could entail differential baseline firing rates in the early visual system. Such a signal might in some way interact with the response to the C1-eliciting probe on a neural level. Although it seems unlikely that such an effect would exclusively drive the modulation of the subsequently-evoked C1 component (and that this would be exclusive to the upper visual field), the current data cannot fully rule out such a possibility. An alternative approach that would have circumvented any such interpretational ambiguity could have been the use of an artificial pupil or dilating eye drops. Although such procedures could involve additional subtle optical effects and would possibly decrease the comparability with the aforementioned studies on attentional C1 modulations, such studies could well represent fruitful extensions of this line of research.

Although our results hence strongly suggest that fluctuations in pupil size can affect C1 amplitudes in a fashion that is independent of

psychological factors like attentional load and emotion, these effects might well co-exist with influences that are implemented on a neural level in early visual cortex, or even on earlier subcortical stages (McAlonan et al., 2008). While it is the case that many studies showing attentional C1 modulations allow for differential pupil sizes between conditions (e.g. Rauss et al., 2009; Rossi and Pourtois, 2012b; Vanlessen et al., 2013), some of them probably did not. For example, one study modulated and probed spatial attention rather than attentional load (Kelly et al., 2008), for which the pupil should not be sensitive as long as both sides of the screen have a similar luminance. In another study that is also unlikely to have featured contributions from differential pupil size, the time between a target stimulus requiring e.g. different levels of attentional load (in an unpredictable event sequence) and the C1-eliciting probe stimuli was too short for the pupil to dilate or contract significantly before the C1 was elicited (Pourtois et al., 2004).

Our demonstration of pupil-size effects on early visual processing raises the question of the functional significance of pupil-size changes that are not just related to mere changes in brightness of the physical stimulation (i.e., the pupillary light response). Previous studies have shown that such cognitive/affective pupil-size changes reflect the tonic and phasic modes of the locus coeruleus (LC) and the norepinephrine system (for a review, see Sirois and Brisson, 2014). In the phasic mode, dilated pupils support a state of focus and exploitation, whereas in the tonic mode, dilated pupils enable task disengagement and exploration. Mechanistically, it has been suggested that such adjustments in pupil size relate to exploration and exploitation through a balance between visual acuity and visual sensitivity. Larger pupils would favor exploration, being more sensitive to weak (and peripheral) sensory

input at the cost of reduced visual acuity. Smaller pupils would favor exploitation, by processing objects at fixation in more detail at the cost of reduced sensitivity for faint peripheral stimuli (Mathot and Van der Stigchel, 2015). As such pupil-size changes would relate to an evolutionary adaptation that allows to adjust visual processing dependent on situational demands (Lee et al., 2014). Large pupils and an expanded field of vision would be more beneficial in life-threatening situations than small pupils and a sharpened focus. Although our data only speak to this question to a limited extent, they do show that pupil size indeed has a direct influence on visual processing, and that this effect already affects the earliest stage of cortical sensory processing in humans.

CONCLUSION

To summarize, we have shown that pupil size has a direct effect on the feedforward response in V1 that is independent of psychological factors like attentional load and emotion, which in turn are themselves believed to also affect V1 activity, but also likely entail differences in pupil size. We think our findings are particularly relevant because pupil-size changes are found in an increasing number of contexts, ranging from arousal, to attentional load, to emotional states, as well as being described in aging and pathological conditions like attention-deficit hyperactivity disorder and autism (Fried et al., 2014; Karatekin et al., 2009; Nuske et al., 2014; Sirois and Brisson, 2014). Our results indicate that in all these conditions and contexts it is important to also consider pupil size when looking at effects on early visual processing.

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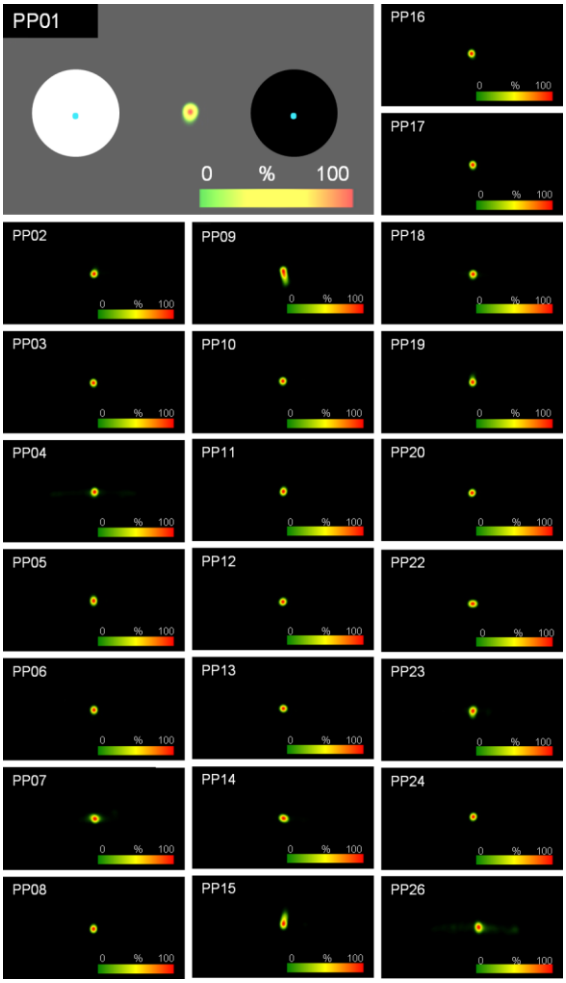
SUPPLEMENTARY MATERIAL



Supplementary Fig 1. Heat maps showing individual overall fixation duration across the visual display (expressed as percentage of overall fixation duration) for all participants in Experiment 1. The black box represents the full presentation screen, and the disc locations are indicated in the panel for participant 1. Relating the heat maps to these positions indicates good fixation quality for all participants.

CHAPTER 4:

REVISITING THE INFLUENCE OF THE PUPIL ON FEEDFORWARD PRIMARY VISUAL CORTEX ACTIVITY: DISCRIMINATING EFFECTS OF ATTENTIONAL STATE AND PUPIL SIZE[1]

We recently demonstrated that pupil size influences the feedforward response in V1 as reflected by the C1 component of the human EEG. This finding is potentially relevant to studies about psychological influences on early visual processing in so far that attentional, emotional, or other psychological modulations often simultaneously dilate or constrict the pupil. In the current study, we tried to replicate this effect and to distinguish it further from possible alternative explanations related to the attentional manipulation (attending a dark or bright stimulus in the lateral periphery) that triggers the pupil-size change. We did this by making use of the slow response characteristic of the pupil by presenting a C1-eliciting probe stimulus at a time point that briefly preceded the pupil response and a time point that followed it. Results showed a replication of the inverse relationship between pupil size and C1 amplitude for probe stimuli at the late time-point but no such modulation at the early time point. Moreover, posterior lateralization of alpha-band oscillatory activity indicative of attentional orienting supported the notion that attention was already deployed to the cued side at the early time point. Together, the present results replicate a recently-described influence of pupil size on feedforward V1 activity, and further support the notion that this effect is indeed directly driven by the modulation of pupil size.

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[1]Bombeke, K., Hopf, J-M., & Boehler, C. N. (under review). Revisiting the influence of the pupil on feedfoward primary visual cortex activity: discriminating effects of attentional state and pupil size. *Psychophysiology*

INTRODUCTION

Primary visual cortex (V1) in the occipital lobe forms the first stage of cortical processing of visual information (Remington, 2012), with its activity strongly reflecting bottom-up processing of visual input (e.g. Engel, et al., 1994; Zhang, Zhaoping, Zhou, & Fang, 2012). Although many studies have shown that feedback signals coming from higher cortical structures also affect activity in this region (Boehler, Schoenfeld, Heinze, & Hopf, 2008; Martinez, et al., 1999; Noesselt, et al., 2002), a long-standing debate concerned how early top-down influences of higher cognitive processes can influence processes in the visual cortex (Spence, 1999). In particular, it is still debated whether the initial feedforward signal through V1 is amenable to top-down influences like attention (Ding, Martinez, Qu, & Hillyard, 2014). Most studies in humans have used EEG to study this question, with the C1 (a central occipito-parietal component between 50 and 90 ms post-probe onset) as an index of V1 processing (Jeffreys & Axford, 1972). Although many studies showed C1-modulating effects of attention (Kelly, Gomez-Ramirez, & Foxe, 2008; Rauss, Pourtois, Vuilleumier, & Schwartz, 2012; Rauss, Pourtois, Vuilleumier, & Schwartz, 2009) or emotional stimuli, states or mood (Pourtois, Grandjean, Sander, & Vuilleumier, 2004; Rossi & Pourtois, 2013; Vanlessen, Rossi, De Raedt, & Pourtois, 2014; Zhu & Luo, 2012), others did not (Clark & Hillyard, 1996; Di Russo, Martinez, & Hillyard, 2003), and maintain that the C1 is not amenable to such influences (Ding, Martinez, Qu, & Hillyard, 2014).

Recently, we have demonstrated that the C1 might be modulated by a very early peripheral effect, namely differential pupil size

(Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016). Notably, many past studies demonstrating attentional and related modulations of the C1 did so in task contexts that might have featured concomitant differences in pupil size, which is known to be modulated by a large number of psychological factors, including attention, effort, emotion, motivation or performance monitoring (for a review, Sirois & Brisson, 2014). In order to demonstrate that pupil size could, in principle, directly modulate the C1 component, we experimentally manipulated pupil size using validated procedures that do not involve differences in luminance or other basic sensory confounds. Specifically, in a first experiment, we used the procedure of Binda, Pereverzeva, and Murray (2013b) in which participants have to covertly attend either a black or white disk (i.e. central fixation), which has been shown to dilate and constrict the pupils. According to Mathot and Van der Stigchel (2015), when covertly attending a white disk, the visual system basically prepares for a saccade towards a brighter image part by triggering pupillary constriction, and the opposite for attending to a dark stimulus. In a second experiment, we used visual illusions of perceived brightness in order to evoke pupil dilation and constriction (Laeng & Endestad, 2012). In both experiments, we presented a typical C1-eliciting probe (Rossi & Pourtois, 2012) after some delay to allow for the pupil to change size. We found in both experiments that the C1 response for upper-visual-field stimulation was smaller for large pupils compared to small pupils. Given that the conditions were matched also for task difficulty, we took this as evidence for a direct influence of pupil size on the C1 response, and suggested basic optical processes as the explanation, in which large pupils are associated with more light aberrations leading to less visual

sensitivity for peripheral stimuli with a high spatial frequency (Campbell & Green, 1965).

Being the first study describing this effect, it still left open a number of possible alternative explanations. Most importantly, although we controlled for luminance differences of stimuli and lateralization of covert attention in our version of the Binda, Pereverzeva, and Murray (2013b) paradigm, one cannot fully exclude an effect of stronger attentional focusing on either the white or black surface of the disk. Here we sought to provide further evidence that pupil size itself affects the C1 component directly. For this, we make use of the sluggish response of the pupil that always responds with a significant delay after the stimulus that prompted a size change (e.g., in the Binda task, attention will have been lateralized already for some time until the pupil-size change occurs), capitalizing on the fact that pupil-size effects would have to follow this slow pace. Based on this, we use two time-points to evoke a C1 response in another version of the Binda task. We selected a relatively early moment (400 ms after disk onset) when attention should already be oriented towards either the dark or bright stimulus but the pupil is not showing a size difference, and a later one (2200 ms after disk onset) at which attention is still in place and pupil size is modulated according to which disk is being attended. We chose the late time-point based on the earlier work showing clear pupil size modulations at this time (Binda, Pereverzeva, & Murray, 2013b; Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016; Mathot, van der Linden, Grainger, & Vitu, 2013). The choice for the early time point was guided by earlier work showing that the pupil size is not modulated yet, while there is already ample time to orient

attention in a pre-cued display (Duncan, Ward, & Shapiro, 1994; Green & Woldorff, 2012; Ristic & Kingstone, 2006; Tipples, 2002). Yet, given the importance that attention is indeed deployed at this time, we planned to further corroborate this through looking at alpha-power asymmetry, which has been reliably linked to lateralized attention (Gould, Rushworth, & Nobre, 2011; Kelly, Lalor, Reilly, & Foxe, 2006; Limbach & Corballis, 2017). Based on this set-up we hypothesized that, if pupil size indeed directly modulates the C1 response, we would find such a modulation for the late time point of probe presentation but not the early one.

METHOD

Participants

We recruited 25 right-handed participants for this experiment (19 ♀). Their ages ranged from 18-26 (mean = 21.64 years, sd = 2.27 years). All of them reported perfect vision (no glasses or contact lenses) and no history of psychiatric or neurological disorders. They provided written informed consent and received a monetary compensation of 25 Euros for an experimental session that lasted two hours in total. Due to technical communication failures between the EEG machinery and the eyetracker or technical problems with one of the two (broken electrodes, overall low signal-to-noise ratio or loss of pupil tracking), data of five participants had to be excluded from analysis. This exclusion took place before any analyses. All procedures were approved by the ethics committee of the Faculty of Psychology and Education Sciences of Ghent University.

Procedure and design

The task was implemented using Presentation® software (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA, www.neurobs.com) on a Microsoft Windows 10 PC with a 24-inch LCD screen. A photo-sensor was used to measure a possible timing delay of the video system, which was found to be constant (1 refresh rate or 16.7 ms). For this experiment, we adjusted our own paradigm (experiment 1 in Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016), which in turn was based on the procedure of Binda, Pereverzeva, and Murray (2013a). Every trial started with three arrows pointing left or right (e.g., <<<) at fixation, followed by the simultaneous lateral presentation of a white and a black disk (11.3° in diameter, centered 10.4° left and right of fixation and presented against a middle grey background) after 300 ms (see Fig. 1). Participants had to covertly orient their attention to the cued side (and hence either the white or the black disk). They were told to keep accurate fixation and to minimize blinking. The online signal of the eyetracker and an additional camera outside the participant room allowed us to closely monitor their gaze, which participants were informed about to discourage their tendency to move their eyes. Nevertheless, when participants made eye movements during the first trials, the experimenter would interrupt the session and restart the experiment after emphasizing the need for accurate fixation. While presenting the disks, task-irrelevant stimulus arrays ("probes") with 22 columns of 6 white horizontal lines were presented in the periphery for 200 ms in order to elicit the C1 component (27.6° x 5.1° of visual angle, vertical distance from closest edge to fixation 6.6°). In order to maximize the number of trials per condition, we exclusively stimulated the upper

VF, which is often the exclusive location to show C1 modulations, both in our earlier work (Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016) and in studies investigating attentional and related modulations of the C1 (Pourtois, Rauss, Vuilleumier, & Schwartz, 2008; Rauss, Pourtois, Vuilleumier, & Schwartz, 2009). The upper VF is represented on the lower bank of the calcarine sulcus (see the "cruciform model", Jeffreys & Axford, 1972), yielding a negative-going C1 components. We randomized and fully counterbalanced the direction of attention (attend left or attend right) and position of the white and black disk across trials (left or right VF). With reference to the onset of the disks, C1-eliciting probes were presented either after 400 ms (50% of trials) or 2200 ms (50% of trials). After 3200 ms, the white and black disks disappeared and were followed by a randomly jittered inter-trial interval ranging in duration between 1000 to 1500 ms.

The experiment consisted of four runs with 240 trials each, separated by breaks (three breaks within a run and one in between runs). Because we anticipated that presenting a C1-eliciting probe shortly after the onset of the black and white disk would result in overlapping vision-related activity, in particular at T1, we tried two different strategies for dealing with such overlap in different blocks. The first two runs had fixed latencies (from now on called 'fixed blocks'), in which the T1 and T2 probe were exactly presented after 400 and 2200 ms, respectively, which was aimed at temporal precision of the two stimulation time-points. Since such a set-up likely entails overlap from the processing of the previous stimuli, we included 80 (1/6) no probe trials. The last two runs had included some temporal jitter of 100 ms around T1 and T2 (uniform distribution; from now on 'random blocks').

In addition to the no-probe trials in the fixed blocks, there were two types of trials: regular and target trials. Regular trials were trials with C1-eliciting probe presentation on T1 or T2. Target trials were trials in which a color change in the center of the disk that participants were covertly attending could occur (change from light blue to yellow, chosen such that the discrimination was similarly difficult in the black and the white disk). For such events, which never occurred in the unattended disk, participants had to press the space bar. This color change could occur before or after the presentation of the C1-eliciting probe, ensuring attentional orienting to the attended disk during the entire duration of the trial. Because the different types of trials were randomly intermixed, participants could not predict target trials. The two fixed blocks jointly contained 320 (4/6) regular trials, 80 target trials (1/6) and 80 (1/6) no probe trials. In contrast, the random blocks contained a total of 400 (5/6) regular trials, 80 target trials (1/6) but no no-probe trials, since we hoped that overlap would be attenuated through the temporal jitter. Both fixed and random blocks lasted 16 minutes, so the experiment had a total duration of 64 minutes.

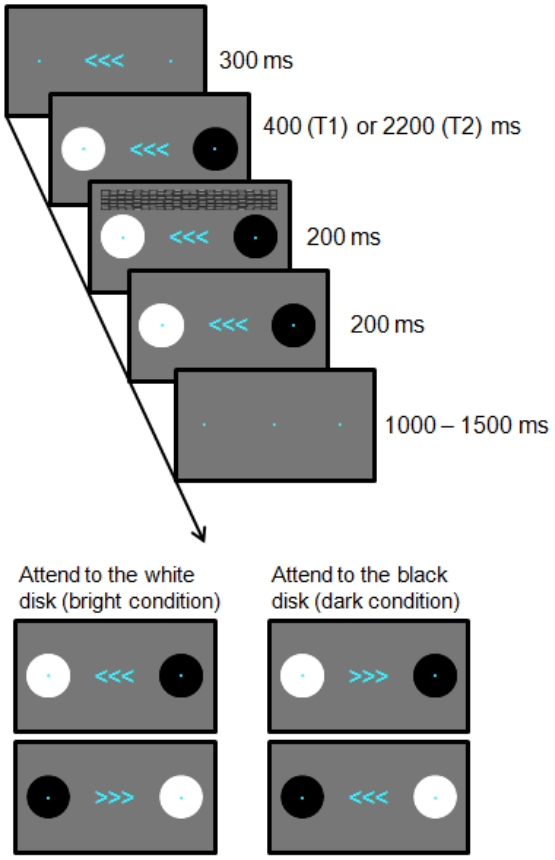

Fig 1. Trial examples specifying durations of the different events. Pupil size was modulated by orienting participants' attention covertly to the white or black disk.

Pupil measurements and preprocessing

We used a 250 Hz SMI eye tracker (RED250 mobile system; SensoMotoric Instruments, Teltow, Germany) to measure pupil size during the experiment. A mobile camera with infrared optics was attached to a standard 17-inch computer screen and a chinrest was used to minimize head movements and to maintain a fixed distance of 65 cm

from the screen. Each block of the experiment started with a calibration procedure in which participants had to follow a moving red dot to nine locations on a grey background. The EEG chamber was dimly lit constantly throughout the experiment. Missing data points due to blinks or recording errors were corrected for by means of a linear interpolation procedure. Trigger codes in both the pupil and EEG data were synchronized with the EYE-EEG Matlab toolbox (Dimigen, Sommer, Hohlfeld, Jacobs, & Kliegl, 2011). Pupil size was initially recorded at a sampling rate of 250 Hz, but then up-sampled to 500 Hz to match the sampling rate of the EEG. The following steps in the pupil analysis were similar to those in EEG analysis. The data was epoched from -500 ms to 2500 ms, time-locked to the onset of the disks and averaged afterwards. Absolute pupil size in millimeters was used in the statistical analysis.

Electrophysiological recordings and preprocessing

EEG data were collected using a Brain Products actiCHamp 64-channel system (Brain Products, Gilching, Germany) with 64 active scalp electrodes positioned according to the standard international 10-20 system, two of which were attached to the left and right mastoids. Signals were recorded with a sampling rate of 500 Hz. During preprocessing, data was re-referenced offline to the average of the mastoids. Next, a band-pass filter of 0.01-30 Hz was applied. The data were epoched from -200 ms to 800 ms, time-locked to the onset of the probe stimuli and baseline-corrected using the 200 ms period preceding probe onset. Automatic artifact rejection was performed on these epochs, removing a small number of trials with extreme peak-to-peak

activity (50 μV) in a subset of posterior electrodes (CPz, Pz, POz, Oz, P1, PO3, P2, PO4). For each participant, less than 10% of trials were excluded, equally distributed across conditions. Next, these epochs were averaged within-subject and a grand average across subjects was calculated for plotting purposes.

Analyses

Pupil size measurements were based on previous work (Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016). We took the average diameter in the window starting 50 ms before (C1-eliciting) probe onset and ending 50 ms after it. It is important to note that the chosen time window captures the pupil size at the moment these probes were presented. The data was split out for early probes (T1; 400 ms after disk presentation) and late probes (T2; 2200 ms after disk presentation). In order to identify the time course and topographic location of the elicited C1, we collapsed the data across all blocks, conditions and participants, leading us to quantify the C1 as the average between 50 and 90 ms over occipito-parietal sites (POz, CPz, Pz, P1, P2) following probe onset. For alpha-band oscillatory activity, we performed a time-frequency analysis on the continuous data using Brain Vision Analyzer's (Brain Products, GmbH, Munich, Germany) complex demodulation function (see Worden, Foxe, Wang, & Simpson, 2000 for a similar approach), which was later epoched (from -200 to 2200 ms, time-locked to the onset of the cue) and baseline-corrected using the pre-stimulus time-range. The same automatic artifact rejection as in the EEG analysis was performed. Depending on the analyses, repeated-measures ANOVAs or two-tailed paired-samples t-tests were used to statistically compare average pupil

sizes, C1 amplitudes and alpha-band oscillatory activity across the experimental conditions. Finally, we calculated Bayes factors for the C1 data at T1 and T2, in particular in order to quantify the support for the null hypothesis for the C1 at T1. Given that we did not find any significant interactions between block type (fixed vs. random) and the experimental conditions for all behavioral, pupil, and EEG measures, the data was collapsed across blocks.

RESULTS

Behavior

In order to compare task difficulty across the different conditions, we ran a repeated-measures ANOVA with factors probe latency (T1 vs. T2) and attended disk color (attending white vs. attending black). For the proportion of correct change detections, both main effects of probe latency and attended disk color were not significant, $F(1,19) = 1.85$, $p = .19$, $r = .3$, and $F(1,19) = 1.11$, $p = .30$, $r = .23$, as was the interaction between probe latency and attended disk color, $F(1,19) = 1.52$, $p = .23$, $r = .27$. The proportion of correct responses was 90% for both change detection in white and black disks at T1 and 88% and 86% respectively for change detection in white and black disks at T2, respectively.

With respect to RT, the main effect of probe latency was non-significant, $F(1,19) = .20$, $p = .65$, $r = .10$, whereas the main effect of attended disk color was, $F(1,19) = 6.77$, $p = .02$, $r = .51$. Yet, the interaction was not significant, $F(1,19) = 2.44$, $p = .14$, $r = .34$. The RT was on average 489 ms and 538 ms for change detection in white and black disks presented at T1, respectively. For probes presented at T2,

the RT was on average 515 ms for change detection in white disks and 528 ms in black disks. Hence, whereas the accuracy parameter suggests similar performance in all four conditions, RT shows slightly faster response times for change detection trials presented while attending the white disk. Although this likely reflects a small difference in task difficulty that we would have liked to avoid (see also Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016), it is important to note that there did not seem to be a significant difference for this effect between T1 and T2.

Pupil size

Cuing participants to attend the white vs. black disk successfully manipulated pupil size and the pattern of results was highly similar to that of our previous work (Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016). Consistent with our earlier work, we first ran a repeated-measures ANOVA with factors probe latency (T1 vs. T2) and attended disk color (attending white vs. attending black) on the mean absolute pupil size in the 100 ms window surrounding the time of probe onset. Both main effects of probe latency, $F(1,19) = 9.59$, $p = .01$, $r = .58$, and attended disk color, $F(1,19) = 61.90$, $p < .001$, $r = .87$, were highly significant, as was the interaction, $F(1,19) = 70.08$, $p < .001$, $r = .79$. Follow-up two-tailed paired-sample t-tests comparing average pupil size while attending covertly to the white or black disk were conducted for probes at T1 and T2 separately. For T1, participants' pupils measured 3.52 mm (SD = .43 mm) in diameter when covertly attending the white disk, and 3.52 mm (SD = .42 mm) when covertly attending the black disk, $t(19) = .63$, $p = .54$. For T2, pupils measured 3.53 mm (SD = .44 mm) when covertly attending the white disk, and 3.64 mm (SD = .44

mm) when covertly attending the black disk, $t(19) = 8.57$, $p < .001$ (see Fig. 2).

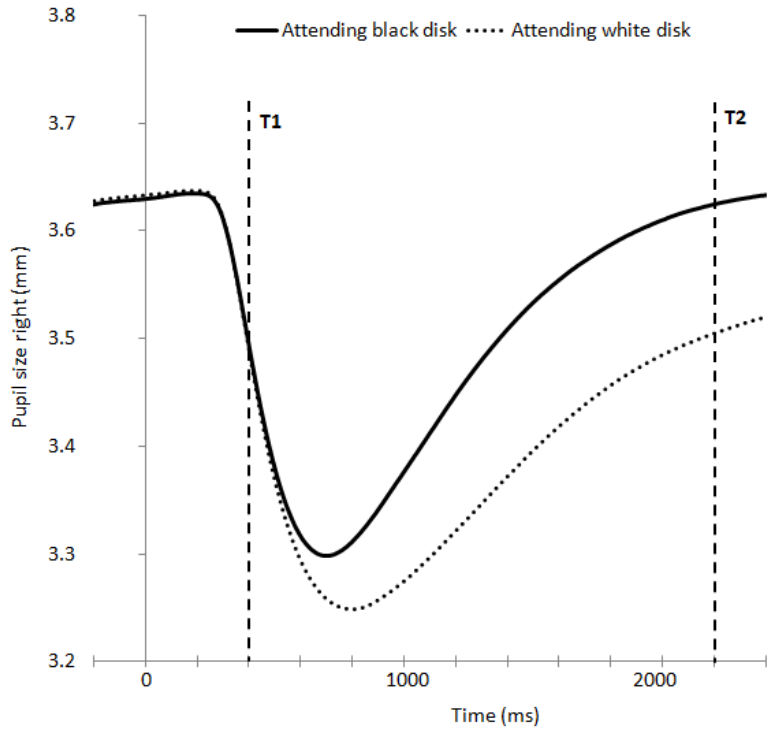

Fig 2. Time course of absolute pupil size in millimeters. Pupil-size was quantified in the 100 ms window surrounding the time of C1 stimulation, indicated by T1 (400 ms) and T2 (2200 ms), showing no difference at T1 and a strong difference at T2.

C1 response

At both T1 and T2, occipito-parietal C1s were evoked by presenting probe stimuli in the upper visual field. Time-range and electrode selection were based on the time course and topography of the overall C1 response, averaged across all conditions (see Fig. 3). This led

us to quantify the C1 with a measurement window of 50 ms to 90 ms post-probe at posterior electrodes POz, CPz, Pz, P1 and P2, after which the topography becomes a bit more anterior before the component completely subsides. Still, the overall C1 response seems to continue a little longer. Yet, exploration of the no-probe trials indicated that this was likely a consequence of the global overlap from disk processing (see below). Moreover, it has been argued that only the earlier parts of the C1 are in fact related to feedforward activity in primary visual cortex (Foxe & Simpson, 2002), so that an early quantification window seems desirable.

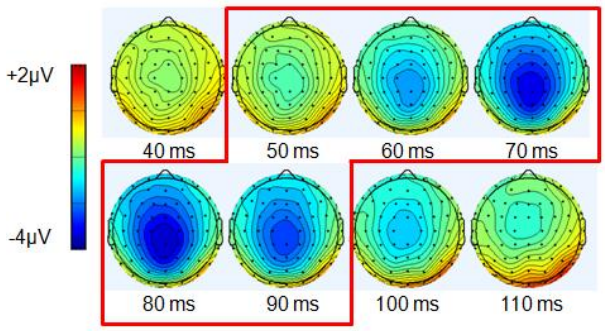

Fig 3. The overall, condition-independent C1 response. Red box highlights the time-window in which the C1 was quantified.

Because comparing the response to two stimuli (disk and probe) at T1 with the response to only one stimulus (probe) at T2 could be problematic due to the residual overlap at T1, we first sought to explore how far this residual overlap might have played a role in bringing about the present results. A strong indication of residual overlap is the sizeable main effect of probe latency that clearly shows that the C1 in

general is much larger at T1 compared to T2 (-3.64 μV vs. -1.41 μV), which seems unlikely to reflect a true difference in the C1 responses evoked by the same sensory stimulus at two different time points. Rather, the increased C1 at T1 is likely to reflect residual processing of the black and white disks, which were presented only 400 ms before T1 in contrast to 2200 ms before T2. Such overlap would be fully preserved in the fixed blocks, and also the 100 ms jitter of T1 probes in the random blocks was probably insufficient to fully attenuate it. In order to corroborate this, we analyzed the 80 no-probe trials in the fixed block to discriminate between disk-related activity and probe-related activity, time-locked to T1 and T2 respectively. As Figure 4 shows, a steep negative-going slope is present for T1 even in the absence of a probe stimulus, but not for T2 (with a difference of 2.63 μV in the C1 window), which identifies residual overlap from disk processing as the likely cause of the large difference between probe latencies on C1 amplitudes. Running a repeated-measures ANOVA with factors probe latency (T1 vs. T2) and attended disk color (attending white vs. attending black) on the mean posterior negative deflection between 50 and 90 ms after the time when the C1 would have been elicited (i.e., analyzing it as a C1) revealed a highly significant main effect for probe latency, $F(1,19) = 23.02$, $p < .001$, $r = .74$ and a non-significant main effect for attended disk color and the interaction between the two, $F(1,19) = .13$, $p = .72$, $r = .08$ and $F(1,19) = .52$, $p = .48$, $r = .16$, respectively. This set of results indicates that residual overlap played a significant role in the overall C1 amplitudes at T1, but not in a differential way across the experimental conditions. Given this clear lack of a differential effect, and since we had

only a limited number of no-probe trials, we decided against using them further for condition-wise overlap removal.

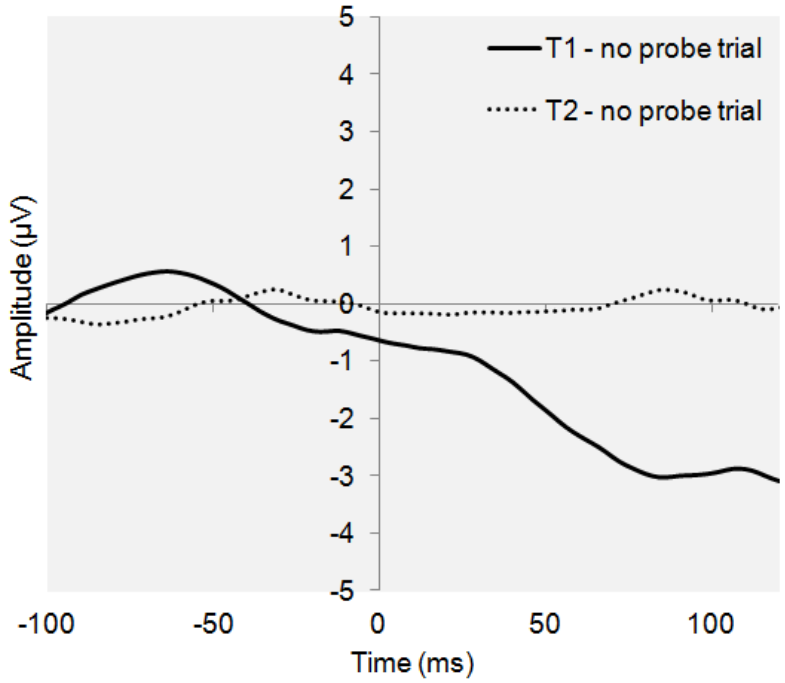

Fig 4. No-probe trials (measured at posterior electrodes POz, CPz, Pz, P1 and P2) time-locked to T1 (without probe stimulation) in the fixed block show a slow decrease in posterior activity, presumably related to the preceding visual processing of the disks.

The above analysis of the residual overlap makes it clear that the evoked response at T1 represents more than just the response to the probe. This basic lack of comparability concerning not just amplitude effects but also sources of variance, led us to perform two-tailed paired-sample t-tests for probes at T1 and T2 separately. Measurements were

performed on the mean posterior negative deflection between 50 and 90 ms post-probe onset. For T1, the C1 measured -3.63 μV (SD = 1.39 μV) when covertly attending the white disk, and -3.64 μV (SD = 1.69 μV) when covertly attending the black disk, t(19) = -.08, p = .94. For T2, the C1 response was -1.59 μV (SD = .98 μV) when covertly attending the white disk, and -1.23 μV (SD = 1.14 μV) when covertly attending the black disk, t(19) = 2.15, p = .04. Hence, we find our hypothesized data pattern of a significant C1 modulation at T2 but not at T1 (Fig. 5).

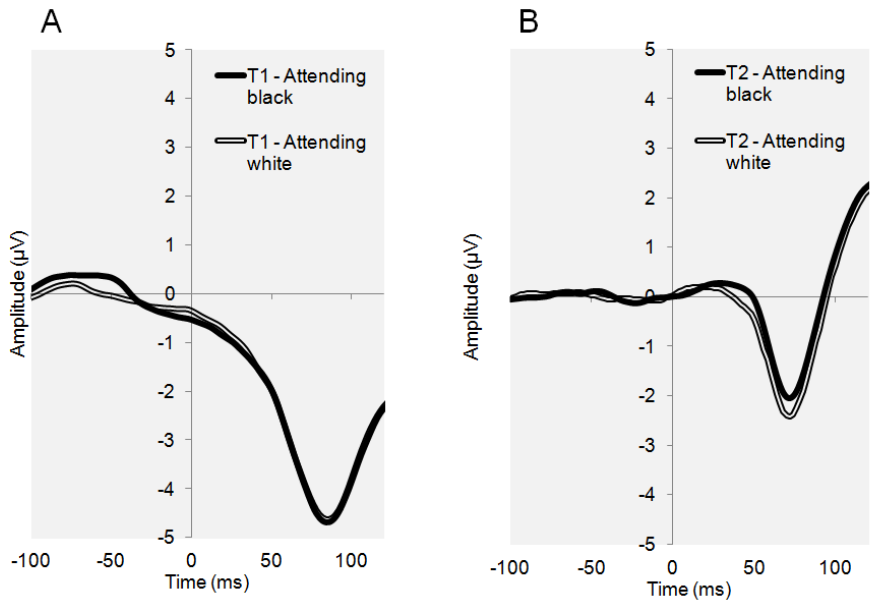

Fig 5. C1 results. Grand-average C1 components (measured at posterior electrodes POz, CPz, Pz, P1 and P2) for T1 (A) and T2 (B).

While this data pattern is in line with our hypothesis, the mere demonstration that one statistical test is significant whereas the other one is not, is problematic (Nieuwenhuis, Forstmann, & Wagenmakers, 2011). We therefore additionally estimated a Bayes factor using JASP software (JASP Team, 2016), in order to quantify in how far we could support the null hypothesis for T1 that there in fact was no difference. This analysis yielded an inverse Bayes factor (BF01) of 4.29 in favor of the null hypothesis for T1, indicating substantial support for the absence of a modulation in T1, according to the guidelines of Jeffreys (1998). Similarly, we found a BF01 of .32 that speaks in favor of the *alternative* hypotheses for T2, reflecting substantial support for the presence of the modulation. Yet another approach to deal with the problem of overlap at T1 was to apply a high-pass filter of 3Hz in order to get rid of the slow oscillations. Filtering T1 but not T2 led to similar C1 amplitudes for both time points, making them more comparible. Running a repeated-measures ANOVA with factors timing and pupil now resulted in a significant interaction between pupil size and timing ($p = .02$) with post-hoc paired samples t-tests showing a non-significant difference at T1 ($p = .16$) and a significant difference at T2 ($p = .04$). Taken together, although we are not sure yet what the approach is to analyze these C1 responses, we think the data seem to support the notion that there is no C1 modulation at T1, in contrast to the likely presence of such an effect at T2.

Alpha-band oscillatory activity

In order to further dissociate between the effect of attentional state and mere pupil size, we measured oscillations in the alpha

frequency range (8-12 Hz) which are known to index participants' attentional state at T1 and T2. That is, lateralized attention to the left or right visual field results in an ipsilateral increase (Foxe & Snyder, 2011) and contralateral decrease of posterior alpha-related activity (e.g. Gould, Rushworth, & Nobre, 2011; Kelly, Lalor, Reilly, & Foxe, 2006), enabling us to investigate if attention was already lateralized at the time of T1 probe stimulation and remained so at T2. Therefore, we performed a time-frequency analysis for which we considered 8-12 Hz as the alpha frequency range, based on previous research (Grent-'t-Jong, Boehler, Kenemans, & Woldorff, 2011; Limbach & Corballis, 2017). The data was binned following a two-by-two design with factors attended disk color (attending white vs. attending black) and attentional lateralization (attending left vs. attending right). Because we were primarily interested in alpha power related to lateralized attentional processing, we decided to only analyze the data from T2 trials in order to avoid sensory responses to T1 probes. Since participants did not know when a target stimulus (or probe stimulus) would be presented, we could look at the T1 and T2 time-points respectively in a fashion that was not confounded by sensory responses at T1. Furthermore, we now time-locked the epochs to the onset of the arrow cue instead of the onset of the disks, since it was likely that lateralized attention could be prepared in the absence of the disks as soon as the participant knew which side to attend. We measured the alpha power at 400 ms and 2200 ms after the onset of the disks. Attention to the right visual field was measured at P3, PO3 and PO7, whereas attention to the left visual field was measured at the mirror locations P4, PO4 and PO8. Afterwards, the resulting left-right differences were collapsed to contra-ipsi differences

for statistical analyses and plotting purposes.

Given the aforementioned lack of comparability between T1 and T2 because of differential overlap from the disks, we again performed paired samples t-tests to check for statistical significance. Collapsing the data across probe latency and disk color showed a marginally significant difference between contralateral and ipsilateral attention, $t(19) = 2.02$, $p = .06$, but note that this two-tailed significance test is rather conservative given the presumed direction of the effect. Split out for T1 and T2, the difference between contralateral and ipsilateral attention was highly significant at T1, $t(19) = -2.68$, $p = .01$, and marginally significant at T2, $t(19) = 1.71$, $p = .1$ (Fig. 6; again note the two-tailed nature of the test). Hence, we find support for our hypothesis that attention is already in place at T1, and this effect seems to stay on quite consistently until T2.

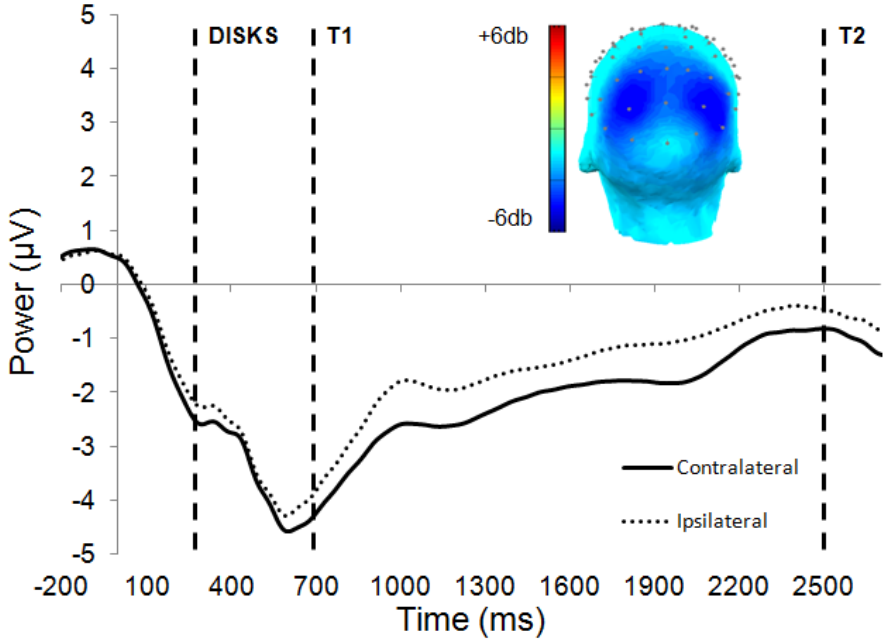

Fig 6. Posterior oscillatory alpha activity measured at contra- vs. ipsilateral to the focus of attention, collapsed across attended disk color. Dotted lines indicate the onset of the disks, probes at T1 and probes at T2 (although no probes were presented at T1 for this subset of data to avoid a sensory response). The topographic scalp map shows the decreased alpha power collapsed across both contralateral and ipsilateral activity.

DISCUSSION

In the present work we replicate and extend our previous demonstration that pupil size can influence the feedforward response in V1 as reflected by the C1 component of the human EEG (Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016). In this earlier study we used stimuli creating a brightness illusion (Laeng & Endestad, 2012) as well as an attentional-cuing experiment (Binda, Pereverzeva, & Murray, 2013b), in which participants either attended a bright or a dark lateral disk stimulus (while the other one was presented on the opposite side). In both cases a change of pupil size led to a C1 modulation, such that a large pupil was associated with a decreased amplitude response. Although this earlier work generally controlled well for differences of physical stimulation across experimental conditions, it was the first demonstration of such an effect, leaving open some alternative explanations. In the present work, we provide further experimental support for pupil size directly influencing the amplitude of the C1 component. (i) We replicate the general effect of an inverse relationship between pupil size and C1 amplitude for probes presented at a time-

point after stimulus onset, where the pupil shows a size difference. (ii) We find no such modulation at an earlier time-point at which pupil size was not modulated yet, but attention was already shifted to the cued side, as verified by a significant alpha-power lateralization at this moment (Limbach & Corballis, 2017).

The rationale of the present study was to investigate the mere effect of pupil size while excluding potential attentional (or related) confounds through dissociating the two processes across two time-points during the task. We decided to focus on the attentional-cuing experiment based on Binda, Pereverzeva, and Murray (2013b) because it yields reliable pupil-size differences and also has a rather well-defined time-line for when they arise. First, we were successful in replicating the pattern of modulating pupil size seen before (Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016): covertly attending a white disk resulted in relative pupil constriction, whereas covertly attending the black disk led to relative pupil dilation. Second, this difference in pupil size was not present at T1. It started 500-600 ms after the presentation of the disks and showed a significant difference at T2. Third, we found evidence that attention was consistently lateralized across both possible probe time-points by looking at hemisphere – lateralized alpha oscillations (8-12 Hz), which are known to index the deployment of attention to lateralized items in the visual field (Foxe & Snyder, 2011; e.g. Gould, Rushworth, & Nobre, 2011; Kelly, Lalor, Reilly, & Foxe, 2006). In line with our expectations, we did find a (small) effect of lateralization with decreased posterior alpha activity contralateral to the attended visual field. This effect did not interact with the pupil manipulation and seemed to continue rather consistently

until T2, indicating a similar attentional state across conditions and time-points.

One aspect we were not completely successful with was equating task difficulty across the different pupil-size conditions. Specifically, in a subset of the trials, participants had to detect color changes in the disk they were attending, and we had strived to make this task equally difficult in the white and the black disk, as was the case in our earlier work (Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016). Although in the present experiment performance was again highly similar in terms of detection accuracy, there was a slight difference in reaction time: people tended to be faster in detecting changes in white disks. While this is not optimal from the perspective of equating the attentional state for the two pupil-size conditions, the small difference in response speed still does not seem to pose a severe problem. On a basic level, since we emphasized accuracy rather than speed when instructing participants, it seems questionable whether participants indeed ended up paying more attention to the dark disks (also because a slight difference in difficulty does not necessarily trigger an increase in attention). More importantly, however, there was no interaction between probe latency and attended disk color, i.e. any subtle difference in attentional state should be similar for the two probe times, for which we find the key dissociation for the C1 (numerically, in fact, the difference is larger at T1, where we did not observe a C1 modulation). Finally, alpha power lateralization did not seem to be differentially modulated by which disk was attended, further suggesting a similar attentional state.

Another point worth discussing is that there was a general lack of comparability between the C1 component evoked at T1 and T2.

Specifically, the former is driven both in amplitude and in variance by an additional stimulus (the disks, and possibly even the preceding arrow stimuli). This was evident when looking at no-probe trials that showed significant residual overlap from these preceding stimuli. Specifically, the C1 was more than twice as large at T1 compared to T2, which seemed to rely strongly on overlap during T1. As such, we had to compare C1 amplitudes within T1 and T2. For T2, we found the expected replication of the effect that a smaller pupil goes together with a larger C1. For T1, we found that they were virtually identical. Yet, in order not to rely on an insignificant t-test alone to infer a null effect (Nieuwenhuis, Forstmann, & Wagenmakers, 2011), we additionally calculated the Bayes factors, which provided substantial support for the null hypothesis, and reported an analysis for which we high-pass filtered the T1 response, making the C1 amplitudes more comparable. Taken together, these results support our main hypothesis that there would be a C1 modulation at T2 but not at T1.

The present data provides critical support for the notion that pupil size directly influences feedforward processing in primary visual cortex. Specifically, the fact that the C1 modulation was present only at a time-point when the pupil-size change had occurred, but not at an earlier time-point where attention was already deployed to the lateralized items, makes it highly unlikely that the C1 modulation reflects attentional state/lateralization, also not as a function of slight differences in task difficulty. Rather, we still deem our previously put forward explanation along the lines of a basic optical aperture effect with more optical aberrations at a large pupil likely (Campbell & Green, 1965) to be most parsimonious. Yet, it is important to note that our

work cannot speak directly to earlier work concerning psychological effects on the C1 (for a review, see Rauss, Schwartz, & Pourtois, 2011), even if such studies might have featured pupil-size differences. Our work only shows in principle that pupil size can influence the C1. Importantly, there are a number of demonstrations of C1 modulations that are very unlikely to have been influenced by pupil size. This applies in particular to studies that, very much like T1 in the present work, elicited the C1 at times when a possible pupil response is unlikely to have happened yet (Kelly, Gomez-Ramirez, & Foxe, 2008; Pourtois, Grandjean, Sander, & Vuilleumier, 2004; Rossi, et al., 2017) or in which pupil size was measured and controlled for (Bayer, et al., 2017).

Finally, the question arises whether the modulation we observe here only reflects an indirect by-product of the locus coeruleus-noradrenergic system (Jepma & Nieuwenhuis, 2011) or also an adaptive mechanism by itself (Mathot & Van der Stigchel, 2015). The present data only suggest that peripheral visual information is represented less accurately when the pupil is large, without it being obvious at this point that this could be adaptive.

CONCLUSION

In the present study, we provide important additional support for the notion that pupil size can directly affect the feedforward flow of visual information through primary visual cortex as reflected by the C1. Specifically, we demonstrate that the C1 is not modulated before the pupil starts to show a size difference across conditions. Importantly, we show that alpha-power lateralization, which indexes attentional

deployment to the cued side of the lateralized display, appears before and after the pupil shows an amplitude difference. This confirms that the C1 modulation associated with the pupil change does not reflect an effect of attention to the target side. In further supporting the observation that pupil size can directly influence C1 amplitudes, the present work further emphasizes the potential relevance of pupil size for the study of psychological influences on early visual processing.

ACKNOWLEDGEMENTS

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CHAPTER 5:

INCREASED EFFORT WITHOUT BEHAVIORAL PAY-OFF: SUSTAINED PUPIL DILATION AND INCREASED ATTENTIONAL PROCESSING IN A REWARDED CONTEXT[1]

Reward manipulations, including sustained ones, have been found to increase task performance and enhance control-related brain activity, in particular in prefrontal cortex in various task domains. At the same time, reward leads to pupillary dilation, which is assumed to be related to neural activity of the locus coeruleus-norepinephrine system. In the present study, we focused on sustained effects of rewarded task contexts on conflict processing in a Flanker task. In half of the blocks, participants received monetary rewards for fast and accurate performance. In contrast to our expectations, we failed to find any behavioral benefits associated with rewarded contexts. Still, we did observe a significant larger posterior negativity related to distracter processing in the rewarded contexts, presumably reflecting a sensory gating mechanism generally boosting the incoming sensory information. Moreover, pupil size was significantly increased in a sustained fashion in rewarded contexts. We interpret the findings in terms of the adaptive gain theory and argue that there can be a dissociation between electrophysiological or pupil-related reward modulations on the one hand and actual task performance on the other hand.

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[1]Bombeke, K., Kostandyan, M., Notebaert, W., & Boehler, C. N. Increased effort without behavioral pay-off: Sustained pupil dilation and increased attentional processing in a rewarded context. *Manuscript in preparation.*

INTRODUCTION

Many studies have shown effects of monetary incentives on both behavioral performance and its underlying neural mechanisms in a variety of task contexts, including conflict processing (Braver, 2015). In paradigms measuring cognitive conflict, participants typically have to overcome stimulus and response conflict by allocating more attention to task-relevant stimulus features while simultaneously suppressing task-irrelevant features (see for example the seminal conflict monitoring model of Botvinick, Braver, Barch, Carter, & Cohen, 2001). Importantly, reward availability can be communicated in different ways: most studies employ cues predicting the potential of reward in the upcoming trial (e.g. Padmala & Pessoa, 2011), whereas other studies directly associate specific task features with reward (e.g. specific rewarded ink colors in Stroop task; Krebs, Boehler, Egner, & Woldorff, 2011; Krebs, Boehler, & Woldorff, 2010). However, reward can also have effects on a longer time scale by creating a motivational context (thereby benefitting all trials that are presented in a block-wise fashion). Comparing large blocks of trials in which reward can be obtained on every trial (given fast and accurate performance) with blocks in which there is no reward to earn, allows to study sustained reward effects (Chiew & Braver, 2014; Jimura, Locke, & Braver, 2010; Langford, Krebs, Talsma, Woldorff, & Boehler, 2016; Massar, Lim, Sasmita, & Chee, 2016; Paschke, et al., 2015; Schevernels, et al., 2015; Small, et al., 2005; Soutschek, Stelzel, Paschke, Walter, & Schubert, 2015; Soutschek, Strobach, & Schubert, 2014). According to Notebaert and Braem (2015), these reward manipulations on the block level presumably influence motivational aspects, whereas performance contingent reward manipulations on the trial level would rather trigger learning responses

and performance non-contingent reward manipulations would lead to affective responses. Jimura, Locke, and Braver (2010), for example, found that a rewarding context in a working-memory task had a sustained effect on the maintenance of goal-related behavior, reflected by changes in behavioral performance (faster responses) and its underlying brain mechanisms (sustained increase in lateral prefrontal cortex activity). Other studies found similar findings, showing increased sustained attention performance in blocks with potential high reward compared to blocks with low and neutral reward (e.g. Massar, Lim, Sasmita, & Chee, 2016) and reward-related increases in parietal and prefrontal cognitive control regions (Locke & Braver, 2008).

In the present study, we wanted to extend these findings on sustained effects of rewarded contexts to conflict processing in a typical cognitive-control task like the Eriksen flanker task. This has been done before in an fMRI context in which a context of potential gain was compared with a context of potential loss (Paschke, et al., 2015). Making use of a flanker task with word stimuli, the authors showed specific patterns of stimulus- and task-related activity for congruent and incongruent trials in both contexts, without discriminating between task-irrelevant and task-relevant stimulus processing. Therefore, we were specifically interested in reward-modulated distracter- and task processing as reflected by attentional event-related EEG components. However, when presenting task-irrelevant (i.e. distracter arrows) and task-relevant (i.e. target arrow) information at the same time, a possible simultaneous enhancement of task-relevant and inhibition of task-irrelevant processes might camouflage each other in the EEG signal. Therefore, we adopted the paradigm of Appelbaum and colleagues in which there was a 200 ms-stimulus onset asynchrony (SOA) between the task-irrelevant and task-relevant information (Appelbaum, Boehler,

Won, Davis, & Woldorff, 2012; Appelbaum, Meyerhoff, & Woldorff, 2009). This 200-ms window allows for an analysis of irrelevant stimulus processing only, before processes related to target processing have begun. In a previous study with a similar paradigm and task design, we found a decreased attention-related visual N1 component in this irrelevant-only time window, which we related to strategic attentional filtering in a context of conflict adaptation (Bombeke, Langford, Notebaert, & Boehler, 2017). This modulation was associated with enhanced performance, since less attention was allocated to the distracting information. Here, we wanted to probe for reward modulation of this component when comparing a rewarded and non-rewarded context.

Besides looking at attentional ERP components related to conflict processing, we were also interested in the effect of a rewarded/motivational context on pupil dilation and its possible role as marker of attentional control. It has been known for a long time that reward and motivation lead to pupillary dilation, presumably by effects on arousal, effort, and attention (Manohar & Husain, 2015; Massar, Lim, Sasmita, & Chee, 2016; Mitz, Chacko, Putnam, Rudebeck, & Murray, 2017). Furthermore, many studies have found that pupil dilation and constriction are inherently related to neural activity of the locus coeruleus-norepinephrine system (for a review, see Eckstein, Guerra-Carrillo, Miller Singley, & Bunge, 2016). According to the seminal adaptive gain theory (Aston-Jones & Cohen, 2005), there is an inverted-U relationship between LC activity and performance on tasks requiring focused attention. Performance would be optimal for moderate levels of LC activity and suboptimal for low and high levels, leading to a drowsy and distractible attentional state, respectively. Similarly, it has been shown that increases in LC activity and hence baseline pupil

diameter are associated with task disengagement or an explorative attentional state, whereas decreases and pupil constriction are associated with task engagement and a more exploitative attentional state (Gilzenrat, Nieuwenhuis, Jepma, & Cohen, 2010; Jepma & Nieuwenhuis, 2011; Unsworth & Robison, 2016; van den Brink, Murphy, & Nieuwenhuis, 2016). Together, this identifies pupil size as an interesting index of attentional state and it has been shown before to be modulated by reward (Massar, Lim, Sasmita, & Chee, 2016).

Hence, we planned to measure both electrophysiological markers of attentional filtering during distracter processing and the sustained effect of reward on pupil size to investigate whether they reflect related cognitive processes. Specifically, we hypothesized that in a rewarding context, less attention would be allocated to the distracter arrows, reflected by a decreased attention-related N1 component time-locked to the distracter. This would be in line with our previous work showing a decreased posterior attention-related N1 reflecting less attentional allocation to the irrelevant information after incongruent trials (Bombeke, Langford, Notebaert, & Boehler, 2017). In contrast, we expected a larger N1 time-locked to the target arrow in the reward context, as far as this can be measured given the overlap of the immediately preceding distractor processing. Second, we expected the distracter-related N1 modulation to be inversely related to the congruency effect, with larger differences in N1 components associated with smaller congruency effects in the rewarding context (and hence improved performance because of reward). Third, a rewarded context should be associated with a sustained increase in pupil dilation, as reflected by a difference in baseline pupil size. Finally, we expected this difference to be a marker of the amount of mental effort or attentional

allocation, predicting the success of attentional inhibition and potentially the size of the N1 component.

METHOD

Participants

For this experiment, 23 participants (7 ♂, 16 ♀, M = 22.9 years) were selected on the basis of an online prescreening questionnaire via the Experimetrix scheduling system (https://experimetrix2.com/rug/). In these questionnaires, people had to indicate their age, gender, handedness and if they had abnormal vision or any neurological disorders. Every interested candidate below 30 years old without abnormal vision (corrected vision was not allowed) and neurological disorders would be invited to subscribe for the experiment via the scheduling system. Before completing the experiment, participants signed an informed consent in which they were informed about their right to stop the experiment whenever they wanted. The procedures were approved by the ethical committee of the Faculty of Psychology and Educational Sciences of Ghent University and participants received 25€ for a session that lasted two hours, plus a variable performance-based monetary bonus of up to 5€. Due to technical problems with the EEG set-up, resulting in an high signal-to-noise ratio, we had to exclude the data of three participants.

Stimuli

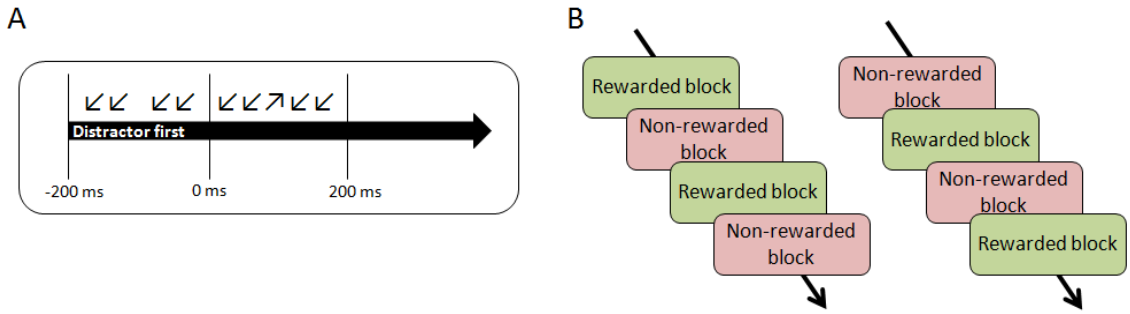
In order to look at attentional processes in cognitive control, we used a variant of the Flanker task with arrows pointing in four different directions (left up, left down, right up, right down). White arrows were

presented on a gray background with a small fixation dot at the center of the screen. Timing was based on Appelbaum, Boehler, Won, Davis, and Woldorff (2012), presenting the irrelevant distracter arrows always 200 ms before the relevant target arrows. This resulted in a "predictable timing" with respect to when the target arrow would be presented. The first independent variable was congruency, so trials could be either congruent (e.g., distracter and target both pointing upwards left) or incongruent (e.g., distracter pointing downwards left and target pointing upwards right). In each block, half of the trials were congruent (four different pairings) and half of the trials were incongruent (twelve possible pairings, distributed evenly).

Procedure and design

Participants were instructed to respond to the direction of the target arrow as fast and accurate as possible. Because of the predictable timing, participants knew that the irrelevant word or distracting arrows would always be presented first. They had to respond by manually pressing one of four keys on the keyboard corresponding to four different arrow directions and they had some time to memorize this response mapping before the start of the experimental phase. The distracter was presented for 200 ms, after which the target arrow was added for another 200 ms. Next, the fixation dot was presented again for 1000 ms in which responses were registered, followed by a jittered response-to-stimulus delay from 900 to 1200 ms (M = 1050 ms). Importantly, participants were informed they would get additional monetary rewards based on a point scheme (+10 points) for each trial when responding fast and accurate in reward blocks. In these rewarded blocks, cumulative reward feedback in the form of the sum of earned points was presented every 20 trials. After the experiment, the total

number of earned points was converted to a monetary reward (maximum of 5 Euros). Participants completed four completely randomized blocks of 128 trials each (64 congruent and 64 incongruent trials) and got a reward for fast and accurate responses in two out of the four blocks (R = rewarded block, NR = non-rewarded block). The presentation order of blocks was counterbalanced across participants (R-NR-R-NR vs. NR-R-NR-R), in order to minimize the influence of



training effects or spill-over effects.

Fig 1. Design of the experiment. (A) On each trial participants were instructed to manually respond to the direction of the target arrow as fast and accurate as possible. Irrelevant distracter arrows would always be presented 200 ms before the relevant target arrow (also presented for 200 ms). (B) Trials were presented in two rewarded blocks and two non-rewarded blocks, counterbalanced across participants. In the rewarded block, participants could earn additional monetary rewards by giving a fast and accurate response.

Behavioral data acquisition and analysis

For RT analyses, the first trial of each block and incorrect or missed responses on trial n were excluded and an outlier rejection criterion of 2 SDs was applied. RT and error rates were analyzed with repeated-measures ANOVAs (rANOVAs), with factors reward context

(rewarded block vs. non-rewarded block) and congruency (congruent vs. incongruent trial). The significance threshold was set to a p-value of .05.

Pupil measurements and preprocessing

We used a 250 Hz SMI eye tracker (RED250 mobile system; SensoMotoric Instruments, Teltow, Germany) to continuously measure pupil size during the experiment. A camera with infrared optics was attached to a standard 17-inch computer screen and a chinrest was used to minimize head movements and to maintain a fixed distance of 65 cm from the screen. Each block of the experiment started with a calibration procedure in which participants had to follow a moving red dot with their eyes to nine locations on a grey background. The EEG chamber was dimly lit constantly throughout the experiment. Missing data points due to blinks or recording errors were corrected for by means of a linear interpolation procedure. Trigger codes in both the pupil and EEG data were synchronized with the EYE-EEG Matlab toolbox (Dimigen, Sommer, Hohlfeld, Jacobs, & Kliegl, 2011). Pupil size was initially recorded at a sampling rate of 250 Hz, but then up-sampled to 500 Hz to match the sampling rate of the EEG. The following steps in the pupil analysis were similar to those in EEG analysis. The data was epoched from -500 ms to 2500 ms, time-locked to the onset of the distracter arrows and averaged afterwards. Absolute pupil size in millimeters was used in the statistical analysis, without applying baseline correction to capture block-level differences.

EEG acquisition, preprocessing and analysis

EEG data were collected using a Brain Products actiCHamp 64-channel system (Brain Products, Gilching, Germany) with 64 active scalp electrodes positioned according to the standard international 10-

20 system, two of which were attached to the left and right mastoids. Signals were recorded with a sampling rate of 500 Hz. The EEG data was analyzed using the EEGLAB (Delorme & Makeig, 2004) and ERPLAB (Lopez-Calderon & Luck, 2014) toolboxes in Matlab. During preprocessing, data was re-referenced offline to the average of the mastoids. Next, a band-pass filter of 0.01-30 Hz was applied. The data were epoched from -200 ms to 1000 ms, time-locked to the onset of the distracter arrows and baseline-corrected using the 200 ms period preceding probe onset. Automatic artifact rejection was performed on these epochs, removing a small number of trials with extreme peak-to-peak activity (150 μV). For each participant, less than 15% of trials were excluded, equally distributed across conditions. Next, these epochs were averaged according to conditions (within-subjects) and a grand average across subjects was calculated for plotting purposes.

The data was split out for rewarded and non-rewarded blocks (2 blocks of 128 trials each). Although the N1 was the main component of interest was N1, we also report P1 measurements. In order to identify the time course and topographic location of the elicited P1 and N1, we collapsed the data across all blocks, conditions and participants, leading us to quantify the P1 as the average amplitude between 100 and 150 ms and the N1 as the average amplitude between 150 and 200 ms. Since there seemed to be both midline and lateral parietal activity, we included both regions in the analyses as a factor region-of-interest (ROI; midline: POz, lateralized: PO7 and PO8). Depending on the analyses, rANOVAs or two-tailed paired-samples t-tests were used to statistically compare average pupil sizes and ERP amplitudes.

RESULTS

Behavioral measurements

A rANOVA with factors congruency (congruent vs. incongruent) and reward context (rewarded block vs. non-rewarded block) on the average RT showed a highly significant main effect of congruency, $F(1,19) = 201.48$, $p < .001$, $r = .96$ but a non-significant main effect reward context, $F(1,19) = .05$, $p = .82$, $r = .05$. The interaction between congruency and reward context was also not significant, $F(1,19)= .57$, $p = .46$, $r = .17$. With respect to accuracy, participants made on average an error in 12% of the trials. The main effect of congruency (congruent vs. incongruent) was again highly significant, $F(1,19) = 40.32$, $p <.001$, $r = .82$, whereas the effect of reward context (rewarded block vs. non-rewarded block) was not, $F(1,19) = .04$, $p = .85$, $r = .04$. The interaction between congruency and reward context was also not significant, $F(1,19) = .34$, $p = .57$, $r = .13$ (see Figure 2).

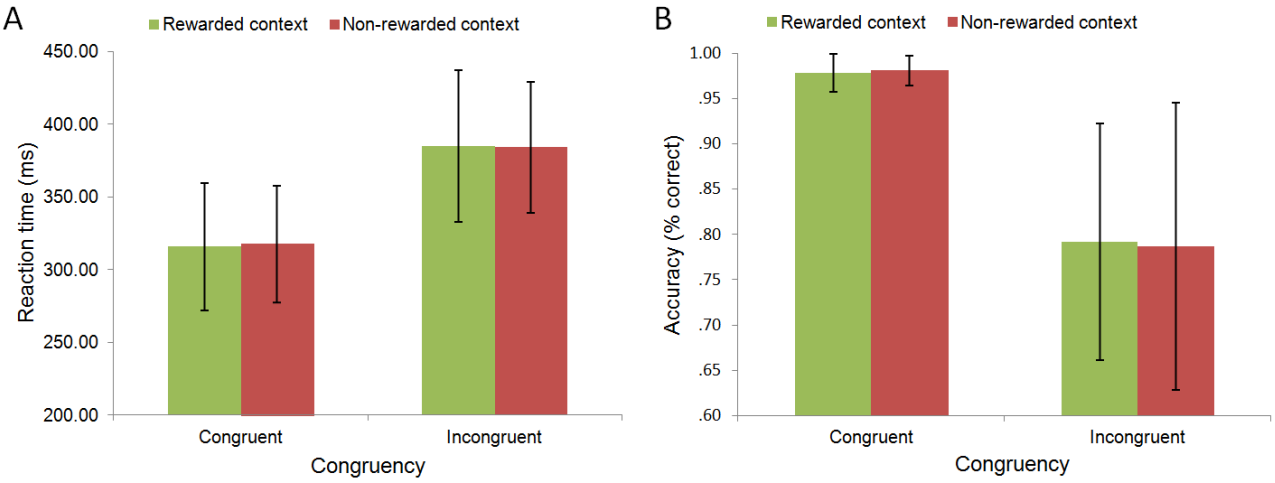


Fig 2. Behavioral analyses. Participants responded significantly faster (A) and more accurate (B) on congruent trials than on incongruent trials. For both RT and accuracy, there was no main effect of rewarded context or an interaction between rewarded context and congruency

Because of the surprising lack of reward effects, we probed the behavioral data further by employing delta-plot analyses and conditional accuracy functions analyses to visualize and compare RT quantiles and to examine whether the experimental manipulation had a larger effect on the relatively fast responses or on the relatively slow ones (Speckman, Rouder, Morey, & Pratte, 2008). Delta plots (Fig 3A) showed that the difference between congruent and incongruent trials was mostly explained by the fast RT trials and that there was an inverse relationship between congruency effect size and RT. Just like in the main analyses, there was no effect of reward context. Conditional accuracy functions (Fig 3B) showed that accuracy for congruent trials was close to 100%, even for the slowest RT trials and that the difference in accuracy between congruent and incongruent trials was again driven

by the fast RT trials. Taken together, we observed no behavioral difference between rewarded or non-rewarded task contexts, neither for plain RT and accuracy measures nor for more detailed distributional analyses that could have revealed more subtle effects.

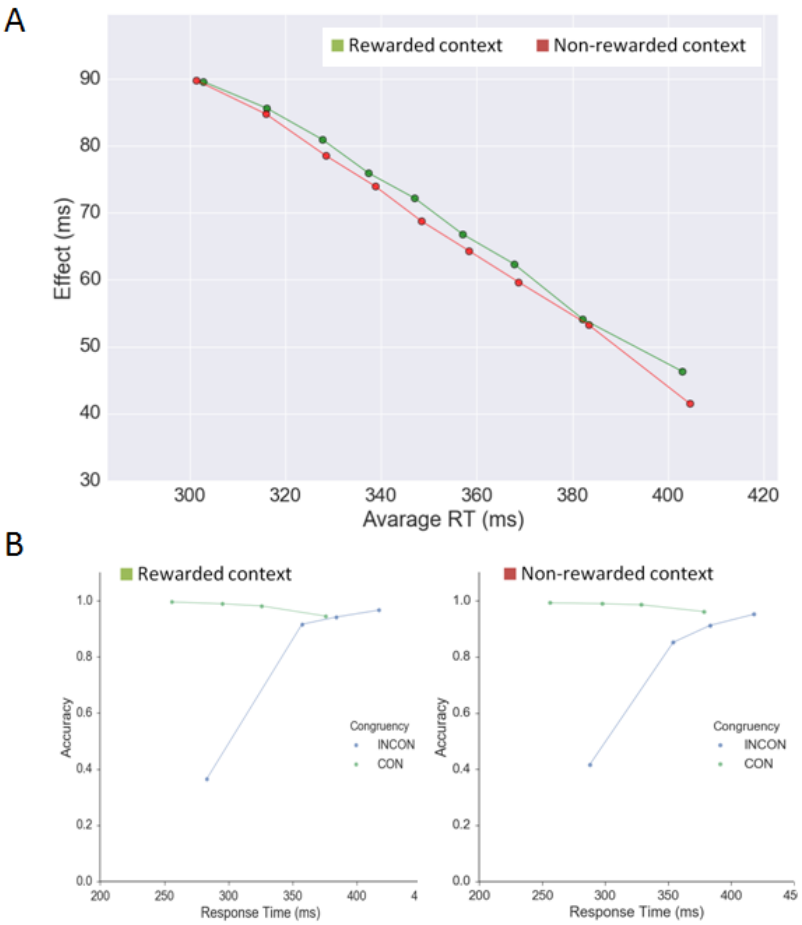


Fig 3. Additional behavioral analyses. (A) Delta plots showing that the reaction time difference between congruent and incongruent trials was mostly explained by the fast RT trials and that there was an inverse relationship between effect size and RT. (B) Conditional accuracy functions primarily showing that the difference in accuracy between congruent and incongruent trials was driven by the fast RT trials.

Pupil size measurements

Sustained pupillary response. In order to analyze the sustained pupillary response, we measured the absolute pupil size from -10 ms to +10 ms, time-locked to the presentation of the distracter arrows, thereby furthermore avoiding the light reflex triggered by the visual stimulation while providing a point estimate of sustained pupil size. Given the general sluggishness of the pupil response, pupil size in this interval could furthermore not be related to the neural processing of the current trial and reflected therefore the general effect of reward context only. Nevertheless, we decided to include the congruency of the current trial in the model for the sake of completeness. A rANOVA with factors congruency (congruent vs. incongruent) and reward context (rewarded vs. non-rewarded) showed the expected non-significant main effect congruency, $F(1,19) = .001$, $p = .97$, $r = 0$, and a highly significant main effect of reward context, $F(1,19) = 26.12$, $p < .001$, $r = .58$. The interaction between congruency and reward context was not significant, $F(1,19) = .81$, $p = .38$, $r = .20$. As shown in Figure 4, absolute pupil size was consistently larger at trial onset in a rewarded context ($M = 5.67$ mm, $SD = 0.86$ mm) compared to a non-rewarded context ($M = 5.49$ mm, $SD = 0.84$ mm).

Transient pupillary response. For the analysis of the transient pupillary response, we measured the mean evoked pupil dilation change for the entire duration of the trial (0 to 2000 ms). Importantly, for this purpose we employed a baseline correction (from -500 ms to distracter onset) in order to exclusively identify transient changes (i.e., Fig. 4 is not reflecting this data in the sense that it was not baseline-corrected). A rANOVA with factors congruency (congruent vs. incongruent) and reward context (rewarded vs. non-rewarded) showed a significant main

effect congruency, $F(1,19) = 5.64$, $p = .03$, $r = .48$ and a non-significant main effect of reward context, $F(1,19) = .40$, $p = .54$, $r = .14$. The interaction between congruency and reward context was not significant, $F(1,19) = .01$, $p = .91$, $r = .03$. In contrast with the sustained pupillary response, the main effect of congruency reflects an increase in pupil size for incongruent trials compared to congruent trials, independently of the reward context. Descriptively, this congruency effect had the expected latency, starting about 800 ms after distracter onset. Since an effect of congruency could hence only show up during the second part of the trial (i.e. 1000 to 2000 ms), we performed an additional analysis on the mean evoked pupil dilation change between 1000 and 2000 ms post-trial onset. A rANOVA with factors congruency and reward context showed a significant (but smaller) main effect of congruency, $F(1,19) = 4.49$, $p = .05$, $r = .05$, and a non-significant main effect of reward context, $F(1,19) = .40$, $p = .54$, $r = .14$. The interaction between congruency and reward context was not significant, $F(1,19) = .01$, $p = .92$, $r = .03$.

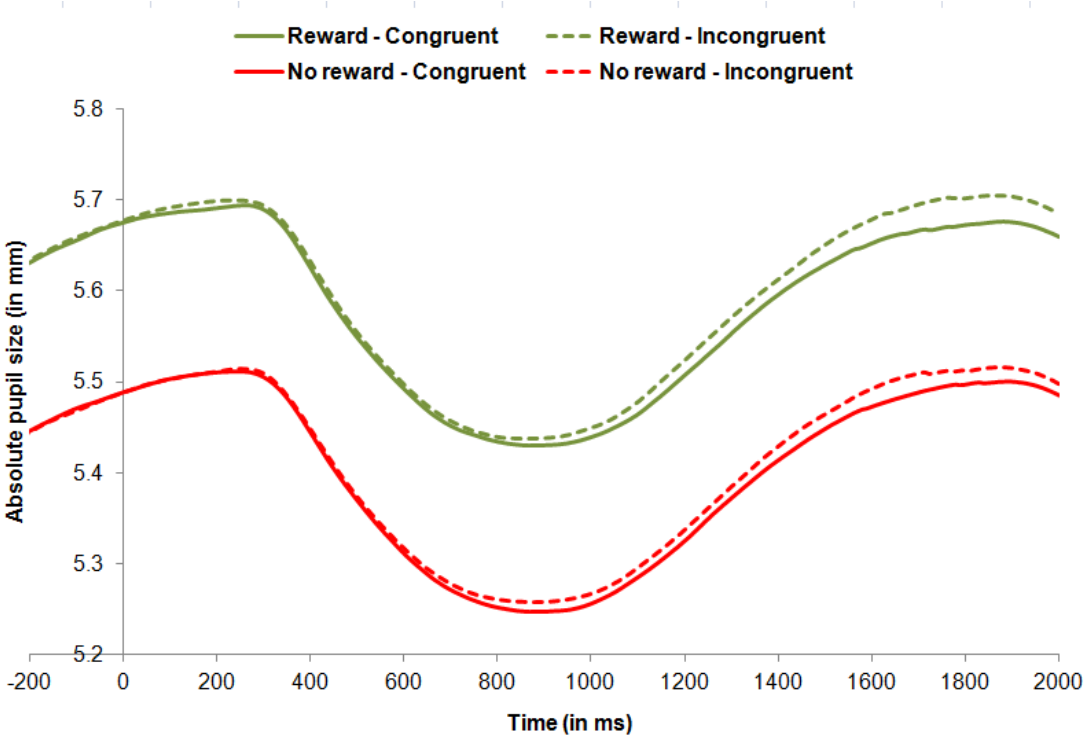


Fig 4. Pupil response. Absolute pupil size (in mm) was consistently larger at trial onset in a rewarded context compared to a non-rewarded context.

ERPs

Distracter-related P1. A rANOVA with factors congruency (congruent vs. incongruent), reward context (rewarded block vs. non-rewarded block) and ROI (midline vs. lateralized) performed on the peak amplitude in a 50-ms window between 100 and 150 ms post-distracter onset revealed no significant main effects for congruency, $F(1,19) = 2.01$, $p = .17$, $r = .31$, reward context, $F(1,19) = 1.53$, $p = .23$, $r = .27$, and ROI, $F(1,19) = 2.04$, $p = .17$, $r = .31$. This lack of congruency effect makes sense, given that the congruency status of the trial could only be determined after the presentation of the target arrow after 200

ms. The two-way interactions between congruency and reward context, F(1(19) = .21, p = .65, r =.10, and between congruency and ROI, F(1,19) = .59, p = .45, r = .17, were also not significant, whereas the interaction between reward context and ROI was highly significant, F(1,19) = 36.14, p < .001, r = .81. Follow-up paired-samples t-tests on the data collapsed across congruency showed a highly significant difference between reward and non-rewarded contexts for the posterior midline ROI, t(19) = -3.12, p < .01 but not for the lateralized ROI, t(19) = .46, p = .65. For the posterior midline ROI, the P1 was larger in a rewarded context (M = 2.01, SD = 3.65) compared to a non-rewarded context (M = 1.34, SD = 3.71), whereas there was no clear difference in the lateralized ROI (rewarded context; M = 2.51, SD = 2.14, non-rewarded context, M = 2.40, SD = 1.87). Finally, the three-way interaction between congruency, reward context and ROI was not significant, F(1,19) = 2.85, p = .11, r = .36.

Target-related P1. Since the central target arrow was presented only 200 ms after the four irrelevant distracter arrows, it was impossible to measure pure target-related EEG acitivity. Therefore, it is important to keep in mind that, whereas the distracter-related early attentional ERPs can only be distracter-related, the target-related ERPs can reflect both distracter and target processing. Nevertheless, a rANOVA with factors congruency (congruent vs. incongruent), reward context (rewarded block vs. non-rewarded block) and ROI (midline vs. lateralized) performed on the peak amplitude in a 50-ms window between 100 and 150 ms post-target onset revealed a highly significant main effect for congruency, F(1,19) = 20.07, p < .001, r = .72, but not for reward context, F(1,19) = .90, p = .35, r = .21, and ROI, F(1,19) = .08, p = .78, r = .06. The two-way interaction between congruency and reward context was marginally significant, F(1,19) = 4.43, p = .05, r =.42,

whereas the interactions between congruency and ROI and reward context and ROI were not, $F(1,19) = 3$, $p = .1$, $r = .37$, and $F(1,19) = 2.02$, $p = .17$, $r = .31$ were not. The three-way interaction between congruency, reward context and ROI also did not reach significance, $F(1,19) = .66$, $p = .43$, $r = .18$.

Distracter-related N1. A rANOVA with factors congruency (congruent vs. incongruent), reward context (rewarded block vs. non-rewarded block) and ROI (lateralized vs. non-lateralized) performed on the peak amplitude in a 50-ms window between 150 and 200 ms post-distracter onset showed significant main effects of reward context and ROI, $F(1,19) = 6.21$, $p = .02$, $r = .5$, and $F(1,19) = 6$, $p = .02$, $r = .49$, whereas the main effect of congruency lacked significance, $F(1,19) = .15$, $p = .70$, $r = .09$. Again, the lack of congruency effect was expected because the congruency status of the trial could only be determined after the presentation of the target arrow after 200 ms. The two-way interactions between congruency and reward context, $F(1,19) = .03$, $p = .87$, $r = .03$, reward context and ROI, $F(1,19) = 3.05$, $p = .1$, $r = .37$, and congruency and ROI, $F(1,19) = .68$, $p = .42$, $r = .19$, were not significant, just like the tree-way interaction, $F(1,19) = .36$, $p = .56$, $r = .14$. Since there were significant main effects for reward context and ROI and the interaction between the two showed a tendency for significance, we ran some additional analyses. Paired samples t-tests showed a significant difference in N1 amplitude between the rewarded and non-rewarded context for the midline electrode, $t(19) = -2.89$, $p = .01$, but not for the lateralized electrodes, $t(19) = -1.69$, $p = .11$. As shown in Figure 5B, there was a more pronounced N1 amplitude (more negative) at POz when trials are presented in a rewarded context ($M = -3.99$, $SD = 3.93$) compared to a non-rewarded context ($M = -2.90$, $SD = 3.35$).

Target-related N1. A rANOVA with factors congruency (congruent vs. incongruent), reward context (rewarded block vs. non-rewarded block) and ROI (lateralized vs. non-lateralized) performed on the peak amplitude in a 50-ms window between 150 and 200 ms post-distracter onset showed significant main effects of congruency and ROI, $F(1,19) = 6.31$, $p = .02$, $r = .5$, and $F(1,19) = 14.26$, $p = .001$, $r = .65$, respectively, whereas the main effect of reward context lacked significance, $F(1,19) = .38$, $p = .55$, $r = .14$. Since both distracter and target arrows were presented at this point, an effect of congruency was possible. The two-way interactions between congruency and reward context, $F(1,19) = 2.14$, $p = .16$, $r = .32$, reward context and ROI, $F(1,19) = 2.30$, $p = .15$, $r = .33$ were not significant, whereas the interaction between congruency and ROI was, $F(1,19) = 6.29$, $p = .02$, $r = .50$. The tree-way interaction did not reach significance, $F(1,19) = .75$, $p = .40$, $r = .19$.

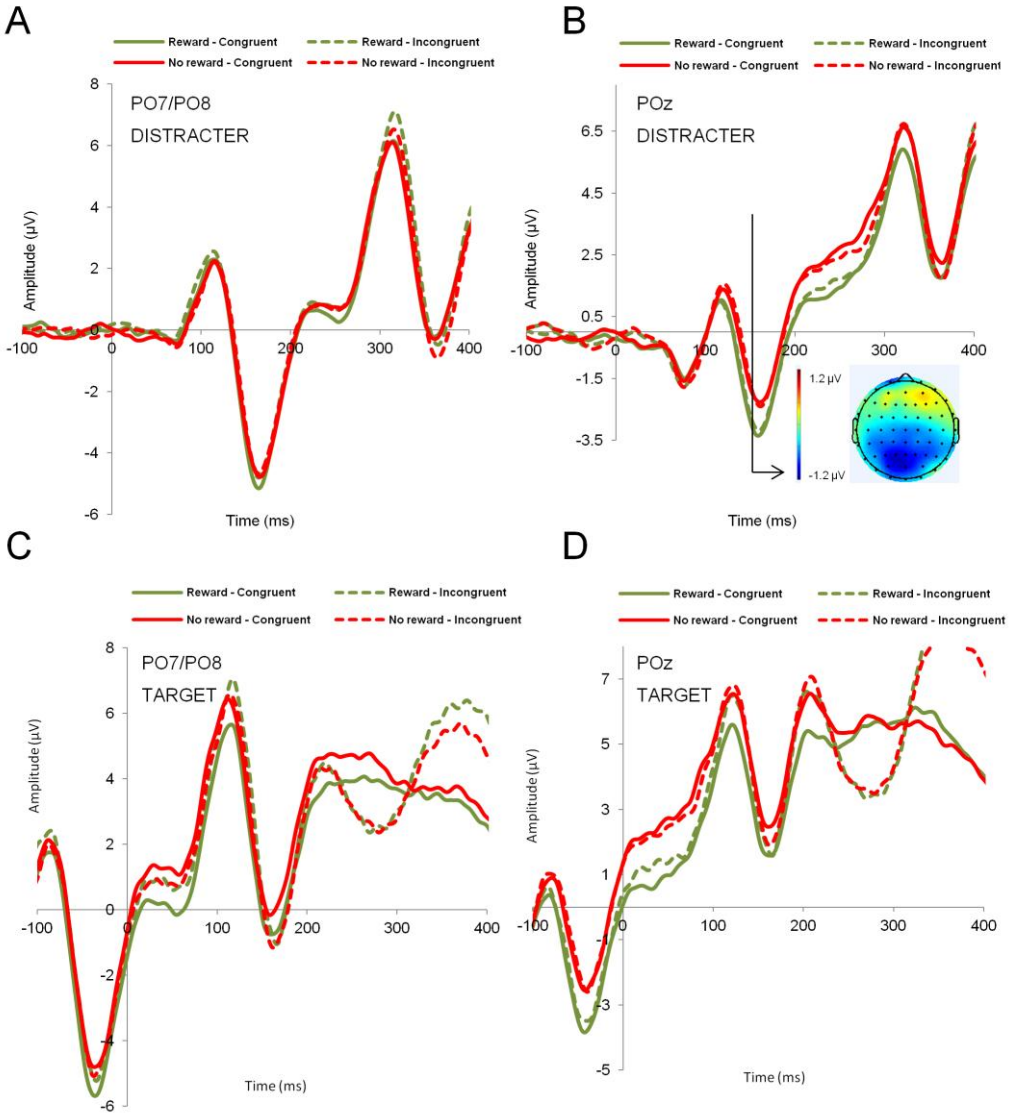


Fig 5. ERP results. (A)(B) For distracter processing, there was a highly significant posterior N1 difference between reward and non-rewarded contexts for the posterior midline ROI (POz) but not for the lateralized ROI (PO7/PO8). (C)(D) For target processing, no significant modulations related to reward context were observed.

Conflict-related N2. Since we expected a shift in latency for the conflict-related N2 component due to the delayed presentation of the target arrow, we visually identified the N2 component using the topographic map across conditions and decided to measure it between 400 and 500 ms post-distracter onset at its typically-found location, the frontal midline electrode FCz. A rANOVA with factors congruency (congruent vs. incongruent) and reward context (rewarded block vs. non-rewarded block) revealed a highly significant main effect of congruency, $F(1,19) = 43.80$, $p < .001$, $r = .83$, and a non-significant main effect of reward context, $F(1,19) = .91$, $p = .35$, $r = .21$. The interaction between congruency and reward context did not reach significance, $F(1,19) = .13$, $p = .72$, $r = .08$.

Correlations. Because we found significant modulations of attention-related ERPs and the size of the pupil, we ran additional correlation analyses (pupil-EEG, pupil-behavior and EEG-behavior. Unfortunately, we failed to find any significant correlation after controlling for multiple testing (all ps > .05). Given the relative low number of participants (N=20), however, this should not be considered as strongly supporting the null hypothesis either.

DISCUSSION

In this study, our goal was to investigate sustained effects of reward contexts on basic conflict processing while measuring different neurophysiologic parameters at the same time. More specifically, we wanted to relate behavioral and electrophysiological markers of attention (P1 & N1 components) to reward-related differences in pupil size, since many studies have found a tight interplay between pupil

dilation and the attention-modulating LC-NE system (Aston-Jones & Cohen, 2005; Aston-Jones, Rajkowski, Kubiak, & Alexinsky, 1994; Eckstein, Guerra-Carrillo, Miller Singley, & Bunge, 2016; Gilzenrat, Nieuwenhuis, Jepma, & Cohen, 2010; Rajkowski, Kubiak, & Aston-Jones, 1994). With respect to reward effects, previous research has shown that when fast and accurate performance in a block of trials is rewarded performance-contingently, there is a sustained increase in proactive control, reflected by enhanced performance and sustained increases in prefrontal cortex activity (Jimura, Locke, & Braver, 2010). The sustained nature of this effect sets it apart from the transient reward effect observed in studies employing reward cues that predict the potential of reward in the upcoming trial (Padmala & Pessoa, 2011) or studies directly associating specific task features with reward (e.g. specific rewarded ink colors in Stroop task; Krebs, Boehler, Egner, & Woldorff, 2011; Krebs, Boehler, & Woldorff, 2010).

In the current experiment, we only had rewarded and non-rewarded blocks and used a Flanker task to present distracter arrows consistently 200 ms before the target arrows (Appelbaum, Boehler, Won, Davis, & Woldorff, 2012). We hypothesized that in a rewarding context, less attention would be allocated to the distracter arrows, reflected by a decreased attention-related N1 component. A decrease in attentional allocation was expected based on previous work of ours (Bombeke, Langford, Notebaert, & Boehler, 2017), showing strategic down-regulation of attention in blocks of trials in which presentation of irrelevant information is temporally predictable. Furthermore, we expected that this N1 modulation would be inversely correlated with a sustained increase in pupil dilation (difference in baseline pupil size), because many studies have found correlations between pupil diameter

and activity in the attention-related LC-NE system (Aston-Jones & Cohen, 2005; Aston-Jones, Rajkowski, Kubiak, & Alexinsky, 1994; Eckstein, Guerra-Carrillo, Miller Singley, & Bunge, 2016; Gilzenrat, Nieuwenhuis, Jepma, & Cohen, 2010; Rajkowski, Kubiak, & Aston-Jones, 1994). This would make the difference in pupil size between the rewarded and non-rewarded block a marker of attentional allocation, potentially predicting the success of attentional inhibition, reflected by the size of the N1 component. With respect to the target arrow, we expected an increased N1 amplitude in the rewarded context compared to the non-rewarded context; yet, the fixed timing of events limited our capability of clearly attributing any activity after target presentation exclusively to target processing.

In contrast to our expectations, we failed to find the behavioral benefits that are usually observed when reward is a block-wise fashion (Chiew & Braver, 2014; Jimura, Locke, & Braver, 2010; Langford, Krebs, Talsma, Woldorff, & Boehler, 2016; Massar, Lim, Sasmita, & Chee, 2016; Paschke, et al., 2015; Schevernels, et al., 2015; Small, et al., 2005; Soutschek, Stelzel, Paschke, Walter, & Schubert, 2015; Soutschek, Strobach, & Schubert, 2014). Participants were as fast and accurate on trials in the rewarded context as on trials in the non-rewarded context and the congruency effect was equally large in both contexts. Follow-up distribution analyses visualizing and comparing RT quantiles suggests that this was partly because of a floor effect for congruent trials, meaning that the task might have been too easy to allow for additional increases in reaction time and accuracy. In line with this, we also failed to find reward modulations of the conflict-related N2 component.

Interestingly, although the reward manipulation did not seem to have an effect on behavior, we did find highly significant effects for the attention-related components and the size of the pupil. More specifically, there was a significantly larger posterior negativity in the rewarded context between 150 and 200 ms after the presentation of the distracter arrows (i.e. before the target arrow was presented). Because of timing and topography, we identified this component as the visual attention-related N1. Somewhat surprisingly, this negativity was only significant at midline electrodes (POz) and not at lateralized channel locations (PO7 and PO8), although the visual N1 is considered to be more pronounced at lateralized regions (Luck, Woodman, & Vogel, 2000; Woodman, 2010). It is therefore possible that the classic N1 component related to selective attention was not modulated by reward context and the posterior midline modulation in fact reflects a more general sensory gating mechanism, in which an increase in attentional allocation results in a boost of the signal-to-noise ratio of incoming sensory information. This would be in line with studies on the role of NE in sensory processing, showing NE-related decreases in spontaneous firing rates (generating neural noise), while sparing stimulus-related signals (Eckstein, Guerra-Carrillo, Miller Singley, & Bunge, 2016; Foote, Freedman, & Oliver, 1975; Waterhouse, Moises, & Woodward, 1980). Moreover, previous research on the relation between the LC-NE system, pupil size and attention (for a review, see Laeng, Sirois, & Gredeback, 2012) has shown that a decrease in sustained LC activity (and hence pupil size) is associated with engaging in a demanding task in which the attentional focus is narrowed down to task-relevant stimuli. In contrast, an increase in sustained LC activity and hence pupil dilation would be associated with a broad attentional focus that is susceptible of task-irrelevant information. Applied to our data, where we observe a

sustained increase in pupil dilation in the rewarded blocks compared to the non-rewarded blocks, this could mean that the larger posterior negativity in response to the distracter is a direct reflection of this broad attentional focus and hence increased attentional processing of the irrelevant information. Furthermore, this could in theory also explain the lack of behavioral benefit in the rewarded contexts since the increase in attentional allocation to the distracters might have increased the reaction time for incongruent trials, counteracting a possible enhanced processing of the target feature associated with monetary incentives. However, since most studies on reward find strong facilitating effects of reward and we do not have a reason to assume this mechanism would only operate under these conditions, this explanation remains speculative.

Although we did not observe an increase in attentional allocation to the target arrows (the main effect of reward was not significant), we suspect that the target was not processed differently than the distracter. In other words, the rewarded context probably led to a sustained increase in attention throughout the trial. This is highly similar to what Schevernels, et al. (2015) found in a rewarded stop-signal task: N1 amplitudes time-locked to the go-stimuli were significantly larger in a rewarded blocked compared to a non-rewarded block. Interestingly, although this heightened attentional state in a rewarded context did not lead to a greater stopping success (and see Langford, Schevernels, & Boehler, 2016, for similar findings), it indicated that attention-related reward modulations can be non-instrumental to the actual performance. Given that we failed to find behavioral benefits of reward, the same phenomenon could be present in our data.

CONCLUSION

Taken together, the results of this study indicate that reward can modulate attention-related ERP components and the size of the pupil without increasing task performance. The non-instrumentality of these processes is remarkable and further research with more optimized design is required to investigate when they do have an effect.

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CHAPTER 6:

MARKER OR MECHANISM: COGNITION-RELATED PUPIL DILATION AND ITS POSSIBLE FUNCTIONAL ROLE[1]

Research in the field of cognitive neuroscience frequently considers lighting-independent changes in pupil size as a marker of internal psychological processes such as attention, mental effort and arousal. The appeal of using pupil size in this way is very obvious, in that it provides a view into psychological processes that are not immediately apparent in behavioral data, and because empirical work has linked pupil size to psychological constructs that are otherwise notoriously difficult to infer (e.g., cognitive effort). Yet, it is striking how this measure is usually exclusively used as a marker of these processes, basically implying that the underlying process is in itself functionally irrelevant. In contrast to this view, we argue here that psychologically-driven variations in pupil size can in fact play a functional role by tipping the scale of an inherent optical trade-off between visual acuity and peripheral sensitivity. As such, we argue that the role of pupil-size modulation that is driven by psychological processes are likely not a pure epiphenomenon of an evolutionary preserved process that has lost its function, but that particularly under natural conditions (i.e., outside of the controlled context of a computer-based laboratory task), the resulting effects are especially likely functionally relevant.

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[1]Bombeke, K., Braem, S. & Boehler, C. N. Marker or mechanism: cognition-related pupil dilation and its possible functional role. *Manuscript in preparation.*

INTRODUCTION

The pupil is highly responsive to incoming light, getting wider in the dark, but narrower in light. The diameter of the pupil therefore has a wide range varying approximately between 1.5 and 9 mm, with an average size of roughly 3 mm under normal lighting conditions (Loewenfeld & Lowenstein, 1999; Sirois & Brisson, 2014). However, even under controlled luminance conditions, pupil size is not constant, and it has been shown frequently to vary as a function of psychological processes that show no direct link to light regulation. Interestingly, most of these studies considered pupil size only as a by-product, epiphenomenon or indirect marker of phenomena related to the autonomic nervous system (for reviews, see Eckstein, Guerra-Carrillo, Miller Singley, & Bunge, 2016; Laeng, Sirois, & Gredeback, 2012; Sirois & Brisson, 2014). For example, pupil dilation increases as function of short-term memory load in a digit-span task, in which participants had to recall 3 to 8 digits (Klingner, Tversky, & Hanrahan, 2011), or as a function of difficulty in a visual search task (Geng, Blumenfeld, Tyson, & Minzenberg, 2015). Because pupil dilation covaries with a wide range of cognitive phenomena and eye trackers have become cheaper and more sophisticated, it is not a surprise that pupil size measurements are growing in popularity every year. Many of these psychological processes are related to activity in the locus coeruleus-norepinephrine system (LC-NE system; Aston-Jones & Cohen, 2005; Aston-Jones, Rajkowski, Kubiak, & Alexinsky, 1994; Eckstein et al., 2016; Gilzenrat, Nieuwenhuis, Jepma, & Cohen, 2010; Rajkowski, Kubiak, & Aston-Jones, 1994), which has been shown to be closely related to pupil size adjustments (Costa & Rudebeck, 2016; Eldar, Cohen, & Niv, 2013; Joshi, Li, Kalwani, & Gold, 2016).

Here, we want to consider pupil dilation from a different point of view and take into account evidence showing that pupil size adjustments themselves change perception. As will be argued below, changes in perception due to pupil size could serve a functional role in optimizing sensory information gathering by either increasing the visual acuity or the peripheral sensitivity. As such, the pupil could be compared to the aperture of a camera lens, constantly automatically regulating the incoming light in order to get the most balanced picture in terms of sharpness and brightness.

Considering a possible functional role of pupil size, evolution usually leads to physiological adaptations in an organism that increase the chance of survival and reproduction, at least at some point in the history of a species. From wrinkly fingers after contact with water (improving grip; e.g. Changizi, Weber, Kotecha, & Palazzo, 2011) to having a short and wide body form when living in arctic climates (conserving heat; e.g. Weinstein, 2005), it is highly likely there was an underlying functional explanation at some point. At the same time, one needs to avoid what is called teleology, wherein each adaptation would be considered a development towards a specific goal (Hanke, 2004). In addition, some adaptations have lost their functionality when they stopped being an advantage for natural selection, but don't necessarily disappear as long as they do not represent an evolutionary disadvantage, a phenomenon usually referred to as "vestigiality". In this paper, we will try to discern whether a functional (or vestigial) role exists for psychologically-triggered pupil-size adaptations.

To set the stage, we will first discuss the different contexts that are known to influence pupil size, including both its primary role in reacting to changing lighting conditions, as well as its responsiveness to different psychological processes. In doing so, we will detail how

research on the latter mainly considered pupil size as a by-product of these cognitive processes without considering a possible functional role. Next, we will briefly review evidence that luminance-driven changes in pupil size also changes our perception and, more importantly, recent evidence suggesting that also psychologically driven variations in pupil size can affect sensory processes. Finally, we will suggest that these sensory changes might indeed play a functional role (as opposed to vestigial) in the context of the psychological processes that trigger them.

WHAT INFLUENCES PUPIL SIZE?

Light regulation

The pupil's most basic and best-known function is light regulation, referred to as the pupillary light reflex (PLR). Visual perception starts with light being reflected off objects in our surroundings, which is projected onto the retinal cells of the human eye. The narrow bands of electromagnetic waves to which our eyes are adapted define our visible light and the perceived color spectrum. The sheer amount of light falling onto the retina is controlled by two antagonistic muscles adjusting the size of the pupil to the current lighting conditions, called the sphincter pupillae and the dilator pupillae (Diamond, 2001; Eckstein et al., 2016; Loewenfeld & Lowenstein, 1999). Considering the underlying mechanism, the PLR is a rather simple brainstem circuit in which increased lighting is detected by the pretectal area (part of the subcortical visual system), triggering the sphincter pupillae to constrict by sending a signal via the Edinger-Westphal nucleus (Ebitz & Moore, 2017; Loewenfeld & Lowenstein, 1999). Although the consensus used to be that this local reflexive pathway could not be modulated by

psychological processes, there is some recent evidence for PLR modulations coming from gaze control areas like the frontal eye field in prefrontal cortex (Ebitz & Moore, 2017).

Psychological processes

Besides the simple brainstem circuit for basic light regulation, pupil size is also controlled by the autonomic nervous system. Pupillary constriction is driven by parasympathetic innervation, whereas pupillary dilation is driven by sympathetic innervation (Loewenfeld & Lowenstein, 1999). Furthermore, it has been shown that both increased activity in the sympathetic 'fight-or-flight' branch and inhibition of the parasympathetic 'rest-and-digest' branch lead to pupil dilation (Bradley, Miccoli, Escrig, & Lang, 2008; Steinhauer, Siegle, Condray, & Pless, 2004). Because of its connections to the autonomic nervous system, pupil size has also been shown to be susceptible to top-down influences of psychological processes like attention, cognitive control and emotion (for a review, see Eckstein et al., 2016; Sirois & Brisson, 2014). It has been demonstrated that the interplay between activity in the autonomic nervous system and changes in pupil size can often be related to the dynamics of locus coeruleus (LC) that is the main source region of norepinephrine (NE) throughout the brain (Aston-Jones & Cohen, 2005; Sara, 2009). It goes beyond the scope of this paper to elaborate on this system (for a review, see Eckstein et al., 2016), but it is important to highlight two profound regularities. The first one is that the temporal coupling between LC activity and changes in pupil diameter is remarkably high (Costa & Rudebeck, 2016; Joshi et al., 2016). The second one relates to the fact that the LC-NE system is involved in many different cognitive processes (Sara, 2009). For these reasons, researchers from different fields have used pupil size as an indirect

marker of activity in higher-order cognition like attention, emotion, language, memory or decision making (for a review, see Eckstein et al., 2016; Sirois & Brisson, 2014). In the following paragraphs, we will roughly distinguish between two main sources of fluctuations in autonomic nervous system activity, namely mental effort and emotional arousal, and their effect on pupil dilation.

Mental effort

Mental effort (or cognitive effort) can be defined as the amount of cognitive resources an individual invests in order to perform a task successfully (Westbrook & Braver, 2015). It should be noted that mental effort is a complex concept that is not only driven by external factors like the difficulty of a task, but also by internal factors like motivation (e.g. when a participant simply decides not to invest effort in a difficult task). It is therefore not surprising that pupil dilation is often used as an indirect measure of mental effort, because it can lead to insights that are impossible to derive from other measures (Boehler et al., 2011). Nevertheless, most psychological models of attention agree that attentional or working memory capacity is limited (for a review, see Coull, 1998) and mental effort therefore heavily depends on the resources left to meet task demands in a specific performance context (Alnaes et al., 2014). A simple example is the number of stimuli in a visual search task: as the number increases, more effort or attentional capacity is required to optimize performance. In this context, it has been found that brain regions known for top-down attentional control and executive functioning interact with the aforementioned LC-NE system (Corbetta, Patel, & Shulman, 2008; Sara, 2009; Sara & Bouret, 2012) and according to the seminal adaptive gain theory of Aston-Jones and Cohen (2005), there is an inverted-U relationship between tonic LC

activity and optimal performance with respect to attentional allocation (i.e. mental effort). In a manner that resembles the classic Yerkes-Dodson arousal curve (Yerkes & Dodson, 1908), high levels of tonic LC activity would be associated with distractibility and an explorative attentional state, whereas low levels of tonic LC activity would be associated with a drowsy and a more exploiting attentional state (Gilzenrat et al., 2010; Murphy, Robertson, Balsters, & O'Connell, 2011). Similarly, task performance would be suboptimal for low and high levels of tonic LC activity, whereas it would be optimal for intermediate levels. Interestingly, the same inverted-U relationship was found between tonic pre-stimulus baseline pupil size and task performance (Gilzenrat et al., 2010; Hayes & Petrov, 2016; Jepma & Nieuwenhuis, 2011; Murphy et al., 2011). Given these findings and the observation of high temporal coupling between tonic pupil size and LC activity, it is not surprising that so many psychological studies measure pupil size as a dependent variable in order to better understand cognition-related brain mechanisms.

Since the list of psychological processes for which pupil size was used as a proxy of mental effort is too long to review here, we give a few examples. For example, it was found that the pupil increases with increasing difficulty in working memory tasks with mental arithmetic (Klingner, 2010). Since the difficultness of a task (i.e. cognitive load) determines how much mental effort is needed, it can be easily estimated by measuring the size of the pupil. Also overcoming cognitive conflict is reflected by the pupil, with increased pupil sizes after incongruent trials compared to congruent trials (Brown et al., 1999; Laeng, Orbo, Holmlund, & Miozzo, 2011; Siegle, Ichikawa, & Steinhauer, 2008; van Bochove, Van der Haegen, Notebaert, & Verguts, 2013; van Steenbergen & Band, 2013). Most models of cognitive control would consider this

pupil-size modulation as a consequence of increased mental effort during incongruent trials (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Silvetti, Seurinck, & Verguts, 2013).

Emotional arousal

The role of the evolutionary old limbic system (with as central brain structure the amygdala) is to mobilize the organism for action in case of threatening events, which it does by increasing activity in the autonomic nervous system (for a review, see Lang, 2014). It is therefore unsurprising that previous research has repeatedly shown effects of emotional arousal on the size of the pupil. Pupillary dilation was not only observed during affective picture viewing (Hess & Polt, 1960; Libby, Lacey, & Lacey, 1973) or affective sound listening (Partala, Jokiniemi, & Surakka, 2000), but also during pain perception (Ellermeier & Westphal, 1995) or aversive learning (Wiemer, Muhlberger, & Pauli, 2014). In addition, pupillary changes related to motivational or rewarding stimuli have been shown to reflect arousal (Chiew & Braver, 2014; Granholm & Steinhauer, 2004), and reward-related pupil dilation was observed in many motivational studies (Bayer et al., 2017; Manohar & Husain, 2015; Massar, Lim, Sasmita, & Chee, 2016; Mitz, Chacko, Putnam, Rudebeck, & Murray, 2017). Also pupil-size changes in response to unexpected events (i.e. cognitive surprise) likely fall into the category of arousal-induced pupillary changes. For example, increased pupil dilation was reported for detecting novel (or "oddball") targets in target detection or gambling tasks (Preuschoff, t Hart, & Einhauser, 2011) or for making unexpected errors in a control task (Braem, Coenen, Bombeke, van Bochove, & Notebaert, 2015).

Taken together, countless studies have used pupil size measurements as indirect marker of activity in a wide range of cognitive processes (Eckstein et al., 2016; Sirois & Brisson, 2014), based on the knowledge that pupil size changes result from fluctuations in autonomic nervous system activity. However, these studies usually do not offer a functional explanation for these changes or at least refrained from discussing whether these changes could in turn affect the cognitive process of interest. In the next section, we will discuss an optical mechanism that has been shown to have an effect on perception and potentially higher-order cognition and that would be a likely candidate to offer a functional explanation for pupillary changes.

WHAT DOES PUPIL SIZE INFLUENCE?

Given the ubiquity with which pupil-size changes are observed in different psychological contexts, the question arises whether such adaptations indeed simply represent a marker of such central-nervous processes, without playing a functional role itself. Below, we will discuss in how far pupil size can, in fact, have a direct influence on visual processing, and speculate in how far such a process could be functionally relevant under the psychological contexts that trigger the pupil-size adaptation. We will dissociate between the well-investigated light-induced changes in pupil size and make the point that the same mechanisms can account for the effect of cognition-induced changes in pupil size.

Effects of light-induced changes in pupil size on perception

Interestingly, light-induced adjustments in pupil size have been long known to have a direct influence on the so-called sensitivity-acuity trade-off (Loewenfeld & Lowenstein, 1999). Specifically, having more or less light on the retina entails an inverse relationship between visual sensitivity (i.e. the ability to detect the presence of dimly lit stimuli in the visual periphery) and visual acuity (i.e. the ability to see stimuli in sharp detail). When there is a lot of light and the pupil constricts, the image falling onto the retina is sharper because the light beams coming from different depths are less refracted and are projected on a smaller surface of the retinal plane, leading to a sharp perceptual image (upper part of Fig. 1). This visual acuity is sacrificed when there is little light and the pupil has to dilate to let in enough light to activate the retinal cells, since light beams are now projected on a larger surface of the retinal plane, resulting in a blurrier perceptual image (lower part of Fig. 1). However, when the pupil is dilated, more light falls on the eccentric rod cells who are responsible for vision at low levels of light, leading to a larger sensitivity for weak stimuli in peripheral parts of the visual field. When the pupil is constricted, mostly the cone cells (responsible for color vision) are activated and the sensitivity decreases (Campbell & Green, 1965; Hirata, Yamaji, Sakai, & Usui, 2003; Laughlin, 1992; Loewenfeld & Lowenstein, 1999).

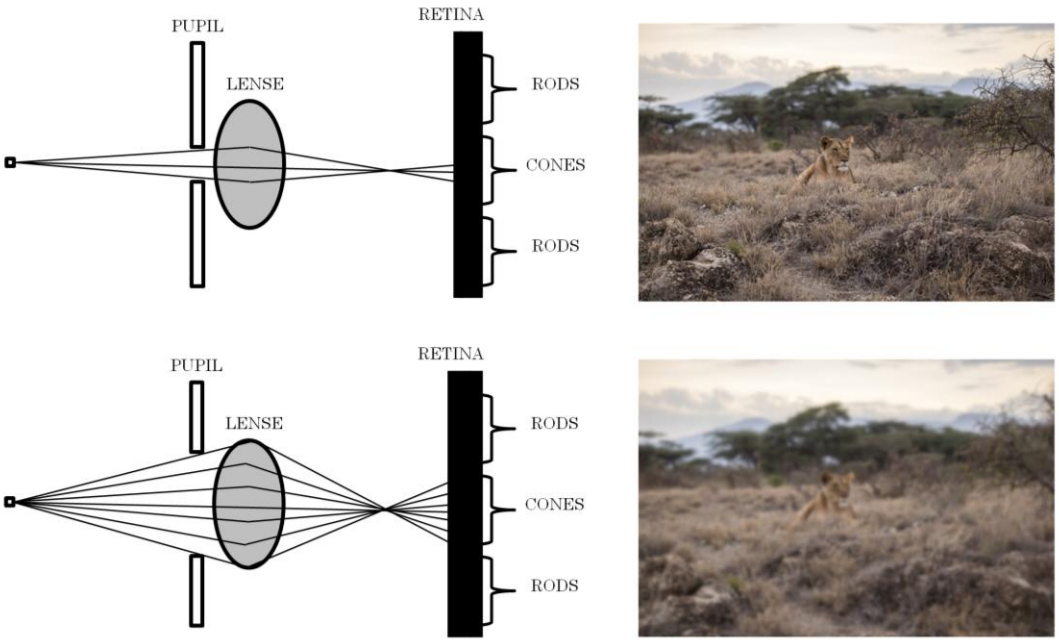

Fig1. Pupillary light regulation and the sensitivity-acuity trade-off.

Effects of cognition-induced changes in pupil size on perception

To determine whether psychologically-induced changes in pupil size could have a similar effect on perception, the literature is in need of systematic ways to influence pupil size in a top-down manner that does not involve (1) changes in light, but also (2) changes in psychological states that could change perception in other ways as well (e.g., differential attentional load). Interestingly, some recent studies have identified such a way in which higher-order cognition can control the size of the pupil, without involving mental effort or emotion inducing processes (Binda, Pereverzeva, & Murray, 2013, 2014; Ebitz & Moore, 2017; Laeng & Endestad, 2012; Mathot & Van der Stigchel, 2015).

First, it was found that covertly attending a dark stimulus leads to pupil dilation, whereas covertly attending a bright stimulus results in

pupil constriction, despite having identical overall physical luminance and mental effort allocation (Binda et al., 2013; Mathot & Van der Stigchel, 2015). Second, a similar effect was found with visual illusion stimuli that elicited an illusory brightness or darkness perception despite equal physical stimulation (Laeng & Endestad, 2012). Mathot and Van der Stigchel (2015) convincingly interpreted the effect in both cases as a prospective top-down retinal protection mechanism: when an ocular movement towards a brighter or darker visual object is imminent, the systems already prepares for a pupil-size change in order to avoid over- or under-stimulation of the retinal cells.

While identifying a centrally-driven mechanism of pupil-size change that could be directly linked to a functional mechanism (adjusting the level of light falling into the eye already prospectively), it does not speculate on additional consequences in the central visual system. In order to probe for such processes, we recently made use of the mentioned paradigms, and showed that pupil size directly influences the feedforward response in the visual system, showing an inverse relationship between pupil size and early primary visual cortex (V1) activity (Bombeke, Duthoo, Mueller, Hopf, & Boehler, 2016; Bombeke, Hopf and Boehler, under revision). We did this by analyzing the C1 ERP component, which is a central occipito-parietal component showing up between 50 and 90 ms after the onset of a visual stimulus and is considered the electrophysiological neural marker of V1 activity. More specifically, we found evidence for a smaller C1 response associated with upper-visual-field stimulation for large pupils compared to small pupils. We interpreted this effect of pupil size on early visual processing in terms of the aforementioned sensitivity-acuity trade-off. Taking into account that an important characteristic of V1 is its sensitivity for sharp edges and high luminance contrast (Nothdurft,

Gallant, & Van Essen, 2000), and the fact that, in order to elicit a clear C1, the C1-eliciting probe stimuli in our study had a high spatial frequency, decreased visual resolution could indeed be a plausible explanation for the observed effect. Moreover, our finding was in line with a study by Daniels, Nichols, Seifert, and Hock (2012), who showed a more blurred retinal image for dilated pupils and a more sharpened image for constricted pupils (i.e. sensitivity-acuity trade-off) in an attentional spread paradigm. Importantly, we did not show that the inverse relationship between pupil size and early primary visual cortex (V1) activity is perfectly linear, since we found comparable C1 effects for rather different pupil-size modulations in our previous work. However, in an attempt to support our claim further that even these small pupil-size modulations are sufficient to have a measurable effect in the visual system, we replicated the effect and additionally showed that the effect could not be explained in terms of attentional confounds (Bombeke, Hopf, and Boehler, in review).

TOWARDS A FUNCTIONAL ROLE FOR PUPIL SIZE IN PSYCHOLOGICAL PROCESSES?

Based on this recent evidence in favor of top-down driven pupillary effects on perception that are likely based on the principle of the sensitivity-acuity trade-off, it seems critical to consider in how far such effects might in fact be functionally relevant in the psychological context under which they arise. Since in many cognitive paradigms trials are presented in quick succession, resulting in slow pupillary changes on trial n-1 still lingering on in trial n, the possibility exists that even slightly altered perception affects the behavioral performance and hence the effects of interest. For example, on a more speculative

note, it might be not a coincidence that low levels of sustained LC activity and hence a drowsy, exploitative attentional state go together with a decreased baseline pupil size and that high levels of sustained LC activity and hence a distractible, explorative attentional state go together with an increased baseline pupil size. It is not unlikely that a moderate sized pupil, reflecting the sweet spot between visual sensitivity and acuity, is optimally tuned in order to achieve the optimal behavioral performance usually found for moderate levels of LC activity (Gilzenrat et al., 2010; Murphy et al., 2011).

Furthermore, studies on the effects of other physiological eye mechanisms than pupil size might provide interesting analogies to how pupil dilation and constriction can play a functional role in perception. For example, Lee, Mirza, Flanagan, and Anderson (2014) found that emotional expressions can directly change the way our eyes gather and focus light because facial muscles and the position of the eyelid change the refractive power of the cornea (Duke-Elder & Abrams, 1970). They argue that emotional expressions like fear (widening eyes) and disgust (narrowing eyes) therefore have a functional role in enhancing either sensitivity or acuity, rather than communicating internal states (or at least not exclusively). Indeed, it was already found that eye widening following fear results in a wider visual field (Susskind et al., 2008) and enhances stimulus discrimination in the visual periphery (Lee, Susskind, & Anderson, 2013) compared to eye narrowing following disgust. Although these studies did not report the respective results, it is highly likely these studies involved differences in pupil size since eye widening leads to increased exposure of the iris (Hedger, Adams, & Garner, 2015; Stamp Dawkins, 1998). It would therefore be interesting to discriminate between the effects of changes in corneal refraction and changes in pupil size during facial expressions and determine their

relative effects on visual processing.

Nevertheless, the question now arises if cognition-related pupil size changes are large enough to have any functional significance or performance benefit for more general cognitive processes. It is a fact that light-related pupil-size changes are much larger than cognition-related pupil size changes (between 2 and 8 mm vs. between 0.1 and 1 mm) and that the few studies showing effects of pupil size on visual acuity only report modest effect sizes (Binda & Murray, 2015; Campbell & Green, 1965). In fact, this made Binda and Murray (2015) predict rather un-measurable effects on visual performance and argue that cognition-related pupil size changes are "vestigial", meaning that they might have lost their original ancestral functionality in humans.

Finally, one possible explanation for why the possible functionality of psychologically-driven pupil-size changes has rarely been considered might relate the limited ecological validity of laboratory tasks. Specifically, it is not unlikely that a heavily controlled laboratory context creates an artificial situation in which the functional effects of pupil size adjustments are underestimated. For example, when an affective picture triggers an emotional arousal response, the pupil will dilate and could in fact have a negative effect on the performance in a perceptual discrimination task in the lab. However, when an emotional event occurs in real life, like hearing the sound of an approaching bear, the dilated pupil will maybe positively affect your chance to detect its location and to run away in the right direction.

CONCLUSION

Taken together, it is remarkable how frequently pupil-size modulations are used as a marker of psychological processes without much speculation whether they represent a functionally relevant process. Given this central role it is playing in various psychological domains, we have tried to systematize the different mechanisms that modulate pupil size and have reviewed the effects that such modulations have on perception. Here we have tried to argue that cognition-related pupil-size changes still play a functional role in human information processing, indirectly affecting perception and subsequent cognitive processes via low-level visual processes like the sensitivity-acuity trade-off. This notion is supported by recent empirical work, but is at this point still somewhat speculative and in need of further corroboration.

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CHAPTER 7:

GENERAL DISCUSSION

"Science works on the frontier of knowledge and ignorance. We're not afraid to admit what we don't know. There's no shame in that. The only shame is to pretend that we have all the answers."

Neil deGrasse Tyson

Although there is a common theme in this dissertation related to early sensory attention and pupil size within the context of cognitive control, a distinction could be made between two main research topics. On the one hand, we were interested in the underlying attentional mechanisms of cognitive control, focusing on the conflict adaptation effect (Chapter 2) and reward-modulated conflict processing (Chapter 5). On the other hand, we were interested in the effect of pupil size on visual processing and the primary visual cortex (Chapter 3 & 4). Furthermore, inspired by our pupil size findings, we wrote a review/opinion paper on the functional role of cognition-induced pupillary changes and its underlying optical mechanisms (Chapter 6).

In this general discussion, we will summarize the studies we performed and highlight their main conclusions, while making a distinction between the two aforementioned research topics. Next, we will try to relate them to each other and make some suggestions for future research.

THE UNDERLYING ATTENTIONAL MECHANISMS OF COGNITIVE CONTROL

Conclusion 1. "An adaptive mechanism based on relative spatial attentional inhibition can be related to conflict adaptation in a context of temporal predictability"

In chapter 2, we focused on the attentional mechanisms of potentially underlying the conflict adaptation effect. This effect describes the phenomenon that the congruency effect (i.e. reaction time or error rate of incongruent minus congruent trials) becomes smaller when the previous trial was incongruent compared to when the previous trial was congruent (Gratton, Coles, & Donchin, 1992). This effect has always been a hallmark of cognitive control research, because it is a prime example of the adaptive and flexible nature of the human control system, primarily involving the anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (dLPFC). Different theoretical accounts were able to explain this effect (for a review, see Duthoo, Abrahamse, Braem, Boehler, & Notebaert, 2014; Egner, 2007), although the majority of researchers were particularly appealed to the conflict monitoring theory by Botvinick, Braver, Barch, Carter, and Cohen (2001). This theory explains the conflict adaptation effect as a monitoring operation wherein the detection of conflict (operationalized as co-activation of different motor responses) triggers a transient increase in selective attention, reducing the amount of conflict experienced in the next trial.

However, in the past decades, surprisingly few studies were able to deliver concrete evidence for these attentional modulations (but see Scerif, Worden, Davidson, Seiger, & Casey, 2006; Suzuki & Shinoda, 2015). Most researche that did study this question used fMRI and found both evidence for enhanced processing of the relevant stimulus

information (e.g. ink color or target arrow) and inhibition of the irrelevant stimulus information (e.g. color word or distracter arrows) (Egner & Hirsch, 2005; King, Korb, von Cramon, & Ullsperger, 2010; Polk, Drake, Jonides, Smith, & Smith, 2008). Unfortunately, fMRI has a very low temporal resolution and the possibility exists that the simultaneous enhancement of relevant and suppression of irrelevant information in a cognitive control task might have camouflaged each other in signals with higher temporal but lower spatial resolution, like the EEG signal. For these reasons, we adopted the EEG-based paradigm of Appelbaum, Boehler, Won, Davis, and Woldorff (2012) in which irrelevant information was presented 200 ms before, at the same time or 200 ms after the presentation of the relevant information. We reasoned that this 200 ms time window would allow for an in-depth analysis of "isolated" markers of sensory processing or attention to the relevant or irrelevant stimulus dimension. We performed two experiments using the Stroop task, and later extended our approach also to the Flanker task. For each type of conflict task, we had one experiment in which the irrelevant stimulus dimension was randomly presented before, after, or simultaneous with the relevant stimulus (ink color or target arrow), and one experiment in which the irrelevant information was always presented before the relevant stimulus.

Hence, the objective of the different experiments was basically to investigate whether an attentional EEG marker of conflict adaptation could be observed in different conflict paradigms optimized for this question. Our main hypothesis was that after an incongruent trial less attention would be deployed to the irrelevant stimulus dimension when presented shortly before the relevant dimension, whereas more attention would be deployed in case the relevant dimension was presented before the irrelevant dimension. Surprisingly, we only found

such a modulation in one out of four experiments, namely in a Flanker task with a predictable irrelevant-first temporal arrangement. More specifically, in that experiment we observed a posterior modulation presumably reflecting a decreased negativity starting around 150 ms that could be viewed as a decreased visual N1 component based on timing and topography or a (conceptually related) selection negativity (Hillyard & Anllo-Vento, 1998). Additionally, this attentional modulation was accompanied by modulations in inter-trial mid-frontal theta power and a theta-power conflict adaptation effect. Therefore, we interpreted the results as evidence for an adaptive mechanism based on relative attentional inhibition under these specific conditions.

In line with the electrophysiological findings, we only found a significant behavioral conflict adaptation effect for trials in which the irrelevant flanker distractors or word names were presented 200 ms before the relevant target. This was very much in line with the studies by Weisman and colleagues (Weissman, Egner, Hawks, & Link, 2015; Weissman, Jiang, & Egner, 2014) who also found that conflict adaptation is the largest when irrelevant distracter information is always presented before the target information. With respect to the lack of conflict adaptation in relevant-first and simultaneous trials, it is possible that participants simply ended up experiencing very little cognitive conflict on trial n, leading to an absence of conflict adaptation effects. This would be in line with the findings of Appelbaum and colleagues (Appelbaum, Meyerhoff, & Woldorff, 2009), showing much larger congruency effects for trials in which irrelevant information was presented first (but see Roelofs, 2010, for alternative findings).

Since theoretical accounts of cognitive control characterized the underlying attentional mechanism of conflict adaptation as a rather general process (Egner, 2007), we did not expect that the attentional

modulation would only show up in the Flanker experiment. One possible explanation relates to the fact that Stroop conflict might mostly rely on feature attention whereas Flanker conflict also involves spatial attention (Luck & Kappenman, 2012). Therefore, it might be the case that the modulation we found is only related to spatial filtering of the visual field (after conflict, less attention is allocated to the visual field on the left and right of the target location), which can explain its absence in the Stroop task. In line with this, the only previous studies investigating the underlying electrophysiological mechanisms of conflict adaptation did report P1 (Scerif et al., 2006) and N1 (Suzuki & Shinoda, 2015) modulations in a sequential Flanker and not a Stroop task. Scerif et al. (Scerif et al., 2006) showed a selective enhancement of the visual P1 component for incongruent trials when preceded by incongruent trials in a flanker task with simultaneously presented distractor and target arrows. No-target flanker trials following incongruent trials were accompanied by a smaller P1 component, which they interpreted as more focused spatial attention. In sum, both our data and the data of the latter study suggest a role for spatial attention in conflict adaptation.

With respect to timing, it can be argued that the experiments with predictable context (i.e. participants knew that the irrelevant dimension would be presented first) probed for proactive control, whereas the experiment with unpredictable context emphasized reactive control adjustments. The fact that we only found a modulation in the predictable context might seem logical, because it would be a disadvantage to employ an attentional filter in the unpredictable context when the subsequent trial would start with the relevant dimension. However, when attentional adjustments would also occur reactively, we hypothesized that such mechanisms would be visible in

the task variants with unpredictable timing, which, however, we did not observe.

Although we believe the four experiments were quite comprehensive, it can be argued that the generalizability of this study is somewhat limited. First, since we only found the modulation for a Flanker task in a predictable context, it is unlikely that this mechanism reflects conflict adaptation in general. Second, with hindsight, we should have probably performed an additional experiment with a predictable context in which the relevant dimension would always be presented first. Based on the current data, we would predict an enhanced N1 after incongruent trials, reflecting more attention to the relevant information. However, presenting task-relevant information always first might have resulted in the absence of congruency effects (and hence conflict adaptation effects), because the participant does not experience any cognitive conflict anymore. Nevertheless, finding a modulation for predictable relevant-first trials would indicate that conflict adaptation is based on a mechanism that both enhances relevant and inhibits irrelevant processing, which would be in line with previously performed fMRI studies (Egner & Hirsch, 2005; King et al., 2010; Polk et al., 2008). Third, although we conducted four completely independent experiments with on average 20 participants, it would have been interesting to perform additional correlational analyses. A correlation between the amplitude difference of the N1 component after incongruent trials compared to congruent trials and the behavioral conflict adaptation effect would be strong evidence that the observed modulation drives conflict adaptation. The same goes for a correlation between the N1 difference and the magnitude of the theta power adaptation effect. Unfortunately, just 20 data points are insufficient to perform reliable correlation analyses on, especially when controlling for

multiple comparisons and correcting for alpha inflation when comparing so many variables. Finally, we did not control for feature integration (Hommel, Proctor, & Vu, 2004) and contingency learning (Schmidt & De Houwer, 2011) processes, which makes it impossible for us to disambiguate between these accounts and to interpret the attentional ERP modulation according to the top-down control or bottom-up learning account. We chose not to do this because such measures would likely decrease the magnitude of the conflict adaptation effect in the different experiment, decreasing the chance to observe ERP modulations in the first place. Furthermore, it is still debated if the distinction between control and learning is as strict as previously assumed, because some authors have argued that learning itself is a control mechanism (Abrahamse, Braem, Notebaert, & Verguts, 2016; Egner, 2014).

Conclusion 2. "Attentional modulations and sustained pupil dilation hinting at increased effort in a rewarded context do not guarantee behavioral pay-off"

In chapter 5 we described an experiment on blocked reward effects and their effects on pupil dilation and attention-related ERP components. Blocked reward effects have been found to increase task performance and to enhance control-related brain activity, in particular in prefrontal cortex (e.g. Jimura, Locke, & Braver, 2010). In this study, we wanted to extend the findings on sustained effects of rewarded contexts to conflict processing in a an Eriksen Flanker task, with a special focus on early attentional modulations and pupil dilation. Specifically, we wanted to relate behavioral and electrophysiological markers of attention (P1 & N1 components) to reward-related

differences in pupil size, since many studies have found a tight interplay between pupil dilation and the attention-modulating LC-NE system (Aston-Jones & Cohen, 2005; Aston-Jones, Rajkowski, Kubiak, & Alexinsky, 1994; Eckstein, Guerra-Carrillo, Miller Singley, & Bunge, 2016; Gilzenrat, Nieuwenhuis, Jepma, & Cohen, 2010; Rajkowski, Kubiak, & Aston-Jones, 1994). Just like in chapter 2, we wanted to take advantage of the high temporal resolution of EEG and discriminate between the processing of the relevant and irrelevant stimulus dimensions (Appelbaum et al., 2012). Therefore, we let participants perform a four-choice Flanker task in which they received monetary rewards for fast and accurate responses in 2 out of 4 blocks of trials (i.e. rewarded blocks or rewarded contexts). Based on the results of the work presented in chapter 2 and in order to increase the amount of cognitive conflict (and the size of the congruency effects), we decided to make the onset of the irrelevant dimension predictable and presented the irrelevant distracters always 200 ms before the relevant target arrows. We hypothesized that in a rewarding context, less attention would be allocated to the distracter arrows and that this would be reflected in a decreased attention-related N1 component time-locked to the onset of the distracter. In contrast, we expected a larger N1 time-locked to the target arrow in the reward context compared to the non-rewarded context, as far as this could be measured given the overlap of the preceding distracter processing. With respect to pupil dilation, we expected that a rewarded context would be associated with a sustained increase in pupil dilation, reflected in increased baseline pupil size, likely relating to increased cognitive effort invested by the participants to maximize their monetary reward (Alnaes et al., 2014; Massar, Lim, Sasmita, & Chee, 2016). Additionally, we were interested in whether the difference in pupil size between rewarded and non-rewarded blocks

could be a marker of the amount of mental effort or attentional allocation, predicting the success of attentional inhibition and potentially the size of the N1 component.

First, in contrast to our expectations, we failed to find the behavioral benefits that are usually observed when reward is a block-wise fashion (Chiew & Braver, 2014; Jimura et al., 2010; Langford, Krebs, Talsma, Woldorff, & Boehler, 2016; Massar et al., 2016; Paschke et al., 2015; Schevernels et al., 2015; Small et al., 2005; Soutschek, Stelzel, Paschke, Walter, & Schubert, 2015; Soutschek, Strobach, & Schubert, 2014). In line with this, we also failed to find reward modulations of the conflict-related N2 component. However, although the reward manipulation did not seem to have an effect on behavior, we did find highly significant effects for the attention-related components and the size of the pupil. More specifically, there was a significantly larger posterior negativity in the rewarded context between 150 and 200 ms after the presentation of the distracter arrows (i.e. before the target arrow was presented), which we could be related to the visual attention-related N1 because of timing and topography. However, surprisingly, this negativity was more pronounced at midline electrodes than at lateralized locations, making it possible that the classic N1 component related to selective attention was not modulated by reward context and our finding in fact reflected a more general sensory gating mechanism in which an increase in attentional allocation resulted in a boost of the signal-to-noise ratio of incoming sensory information (Eckstein et al., 2016; Foote, Freedman, & Oliver, 1975; Waterhouse, Moises, & Woodward, 1980). This finding was contrary to our expectations, since we expected to observe reward-related strategic inhibition of the distracter. In addition, although we did not observe an increase in attentional allocation to the target arrows, which might have been

because of overlap from distracter processing, we assume that the target was not processed differently from the distracter. Therefore, we concluded that the rewarded context led to a sustained increase in attention throughout the trial, and suggest that it might not be possible for participants to differentially deploy attention to different stimulus dimensions that arise in such rapid succession.

However, besides the lack of behavioral reward effect, our study had some more limitations. First, the simple design of the experiment (only distracter-first trials in a rewarded or non-rewarded block) did not allow for an analysis of transient reward effects, which would have been interesting with respect to within-block transient pupil size changes. Previous research has shown that there is a transfer of reward effects to non-rewarded trials in a rewarded block (Jimura et al., 2010) and it would therefore have been interesting to compare N1 components related to distracter processing in rewarded and non-rewarded trials within a rewarded context. Manipulating reward availability on the trial level would also have allowed us to compare sustained and transient pupil responses, which is rather uninformative in the present study. However, in this context, it is interesting to note that when we accounted for the block effects by baseline correction, we did not observe transient effects of pupil dilation. Second, when analyzing the target-related attentional ERP components, baseline correction because of the overlap from the components evoked by the distracters. We tried to solve this by choosing the baseline in the 200 ms interval before distracter processing, but it is still problematic to compare the P1 and N1 components related to the distracter arrows to those related to the target arrow due to likely overlap from distracter processing. Future work could for example include distracter-only trials to counteract this problem by subtracting the estimated overlap.

Theoretical implications for cognitive control research

In both the study on conflict adaptation and the study on sustained reward processing, we were able to identify an electrophysiological marker of distracter processing in the context of cognitive control. More precisely, we found negative-going posterior modulations at the time the N1 is usually observed (but note that their exact nature might be different because they were most prominent at different electrode locations). When framing these findings within the aforementioned DMC or "dual mechanisms of control" framework, which proposes a proactive and reactive operating mode of cognitive control (Braver, 2012; Braver, 2015), it can be argued that both modulations reflect proactive control processes. In the conflict adaptation study, the proactive nature was reflected in the fact that we only observed it in a predictable condition (i.e. irrelevant will be presented first). In the reward study, the combination of a predictable trial course and a context of potential reward created the proactive urge to optimize attention during distracter processing. Nevertheless, the efficiency or functionality of the modulation with the goal of optimizing task performance was contradictory: whereas the attentional modulation increased the chance of not being distracted by the distracter arrows in the conflict adaptation experiment, the opposite was true for the sustained reward experiment. Although it is rather artificial to directly compare both experiments, it highlights that reward can also have non-instrumental effects. This is in line with research of Schevernels et al. (2015) and Langford, Schevernels, & Boehler (2016), for example, who reported larger N1 amplitudes for go-stimuli in a

rewarded blocked compared to a non-rewarded block in a rewarded stop-signal task that did not lead to a greater stopping success.

THE EFFECT OF PUPIL SIZE ON THE PRIMARY VISUAL CORTEX

Conclusion 3. " Pupil size can have a direct effect on the feedforward response in V1: a large pupil leads to decreased activity"

While studying the neural mechanisms underlying the conflict adaptation effect, we realized that previous congruency is just one factor affecting the current trial. Because pupil dilation related to mental effort (or related processes) is also observed in conflict paradigms (Laeng, Orbo, Holmlund, & Miozzo, 2011), we hypothesized that a dilated pupil on trial n-1 could potentially affect the processing of trial n and affect control adjustments like the conflict adaption effect. Hence, although chapter 3 is not a direct follow-up on the work in chapter 2, it acted as a source of inspiration. Before looking at higher-order cognitive processes like cognitive control, we decided to study the effect of mere pupil size on low-level visual processing first, focusing on the primary visual cortex located in the occipital lobe of the posterior brain. The primary visual cortex can be considered the first main stage of cortical visual processing, primarily reflecting bottom-up processing of visual input (e.g. Engel et al., 1994; Zhang, Zhaoping, Zhou, & Fang, 2012). Within the visual cortex, an anatomical and functional distinction can be made between the striate visual cortex (primary visual cortex or V1) and the extrastriate visual cortex (V2, V3, V4, V5). Although many researchers agree that top-down processes can modulate relatively early stages of the extrastriate visual processing (Boehler, Schoenfeld, Heinze, & Hopf, 2008; Clark & Hillyard, 1996; Martinez et al., 1999;

Noesselt et al., 2002), other researchers have found that also striate cortex (i.e. V1) can be modulated by showing effects of attention (Rauss, Pourtois, Vuilleumier, & Schwartz, 2012; Rauss, Pourtois, Vuilleumier, & Schwartz, 2009) or emotions (Pourtois, Grandjean, Sander, & Vuilleumier, 2004; Rossi & Pourtois, 2013; Vanlessen, Rossi, De Raedt, & Pourtois, 2014). Such work on striate cortex effects has been mostly studied by looking at the C1 component (i.e. the first visually evoked potential) as index of V1 processing (Jeffreys & Axford, 1972).

In order to investigate possible bottom-up effects of pupil size on visual processing, we experimentally manipulated pupil size using validated procedures that did not involve differences in luminance or other basic sensory confounds. In a first experiment, we used the procedure of on Binda, Pereverzeva, and Murray (2013) in which participants had to covertly attend either a black or white disk (i.e. central fixation), which has been shown to dilate and constrict the pupils. In a second experiment, we used visual illusions of perceived brightness in order to evoke pupil dilation and constriction (Laeng & Endestad, 2012). In both experiments, we presented a typical C1-eliciting probe (Rossi & Pourtois, 2012) after some delay (i.e. 1800, 2200 or 2600 ms) to allow for the pupil to change size. First, we successfully obtained the intended pupil response: covertly attending a black disk or fixating the dark illusion made the pupils dilate, whereas covertly attending the white disk or fixating the bright illusion made the pupils constrict. Second, we did not observe significant differences in detecting faint color changes in a subset of trials in the experiment based on Binda et al. (2013), indicating equal allocation of attentional effort between conditions. Third, and most interestingly, the results showed that pupil size directly affected the C1 response. More precisely, we found that the response to a C1-eliciting probe in the upper visual field

elicited a smaller C1-amplitude when the pupil was large compared to when the pupil was small. We interpreted this effect of pupil size on the C1 response in terms of the sensitivity-acuity trade-off. This trade-off refers to the fact that having more or less light on the retina entails an inverse relationship between visual sensitivity (i.e. the ability to detect the presence of dimly lit stimuli in the visual periphery) and visual acuity (i.e. the ability to see stimuli in detail). When there is a lot of light and the pupil constricts, the image falling onto the retina is sharper because the light beams coming from different depths are less refracted and are projected on a smaller surface of the retinal plane, leading to a sharp perceptual image. This visual acuity is sacrificed when there is little light and the pupil has to dilate to let in enough light to activate the retinal cells, since light beams are now projected on a larger surface of the retinal plane, resulting in a blurrier perceptual image (Loewenfeld & Lowenstein, 1999), a process that at its extreme end means that you are not allowed to drive your car when an ophthalmologist used pupil-dilating eye-drops on you. Taking into account that an important characteristic of V1 is its sensitivity for sharp edges and high luminance contrast (Nothdurft, Gallant, & Van Essen, 2000), and the fact that, in order to elicit a clear C1, the C1-eliciting probe stimuli in our study had a high spatial frequency, decreased visual resolution could indeed be a plausible explanation for the observed effect.

Conclusion 4. " It is unlikely that the effect of pupil size on the feedforward response is confounded with attention or mental effort"

Since the effect of pupil size on the C1 response was a highly novel finding with potentially far-reaching implications for studies involving concomitant pupil size changes, we decided to do a follow-up

study. Hence, in chapter 4, we tried to replicate the effect and to distinguish it further from possible alternative explanations related to the attentional manipulation (attending a dark or bright stimulus in the lateral periphery) that triggered the pupil-size change in experiment 1 of the first study. Although physical stimulation did not differ between conditions (because participants were always fixating the middle of the screen) and the side of presentation was counterbalanced across left and right, one could argue that "attention to a bright surface" or "attention to a dark surface" would result in some kind of a central cognitive state explaining the C1 effect.

Because this alternative explanation for our effect was not applicable to experiment 2 of chapter 3 (centrally attending brightness illusions), we decided to only redo the first experiment. In order to approach this question, we made use of the slow response characteristic of the pupil to present a C1-eliciting probe stimulus at a time point that briefly preceded the pupil response (T1; 400 ms after disk onset) and a time point that followed it (T2: 2200 ms after disk onset). In addition, we looked at EEG alpha-lateralization as an index for attentional deployment and again compared the behavioral performance on a subset of catch trials. The results showed a replication of the effect of an inverse relationship between pupil size and C1 amplitude for probes presented at a time-point where the pupil shows a size difference (T2). Crucially, we did no find such modulation at an earlier time-point (T1) at which pupil size was not modulated yet. Additionally, significant alpha-power lateralization showed that attention was already shifted to the cued side at T1, supporting an explanation in terms of mere pupil size and not attentional state or allocation.

Conclusion 5. " Psychologically-driven variations in pupil size can probably play a functional role by tipping the scale of an inherent optical trade-off between visual acuity and peripheral sensitivity."

Our work presented in chapters 3 and 4 showed that mere pupil size can in all likelihood have an effect on early sensory processes in the visual cortex. This inspired us to write an opinion paper/review on the often-ignored possible functional role of pupil size in studies considering lighting-independent changes in pupil size as a marker of internal psychological processes such as attention, mental effort and arousal. The appeal of using pupil size relates to the fact that it provides a view into psychological processes that are not immediately apparent in behavioral data, and because empirical work has linked pupil size to psychological constructs that are otherwise really difficult to operationalize (e.g. cognitive or mental effort; Alnaes et al., 2014; Massar et al., 2016). We thought it is striking how this measure is usually exclusively used as a marker of these processes, implying that the underlying process itself carries important information but is in itself functionally irrelevant. In contrast, we argued that the role of psychologically-driven pupil-size modulation relates to a mechanism called the sensitivity-acuity trade-off, in which the size of the pupil determines both the sharpness or visual resolution of the retinal image and the ability to detect peripheral or faint stimuli.

A case for simultaneous EEG and pupil data acquisition in cognitive control research

The work in this dissertation has hopefully illustrated that there can be an interesting interplay between pupillary adjustments and visual evoked potentials. Therefore, we think that future research should continue to measure both simultaneously in order to better understand the subtle effects of optical characteristics of the eye on the ERP component (or EEG frequency) of interest. Because cognitive control research usually entails a typical trial structure in which a temporary discrimination can be made between the pre-stimulus baseline, the stimulus onset, the stimulus-response interval and the inter-trial interval, there are many possibilities to investigate the inter-related dynamics of behavioral, pupillary or EEG-related markers of perception, attention, memory or decision making (see Fig 1 for a visual illustration). Hong, Walz & Sajda (2014), for example, conducted an auditory oddball task and found that baseline pupil diameter correlated with early and late variability in EEG components, supporting evidence for a linear relationship between baseline LC-NE activity and evoked EEG. Moreover, they showed that pre-stimulus alpha activity showed a negative linear relationship with evoked pupil dilation, likely showing that more attentional involvement (i.e. decreased alpha) before the trial starts leads to increased post-stimulus LC activation. A similar approach could be extended to cognitive control research when investigating sequential effects like the conflict adaptation effect. Of course, in order to successfully perform such an analysis, a data-driven approach with single-trial variability is imperative. In this dissertation, we stuck to the traditional approach of averaging across trials and

running ANOVA models, but it would have been interesting to analyze the data with these more advanced models as well.

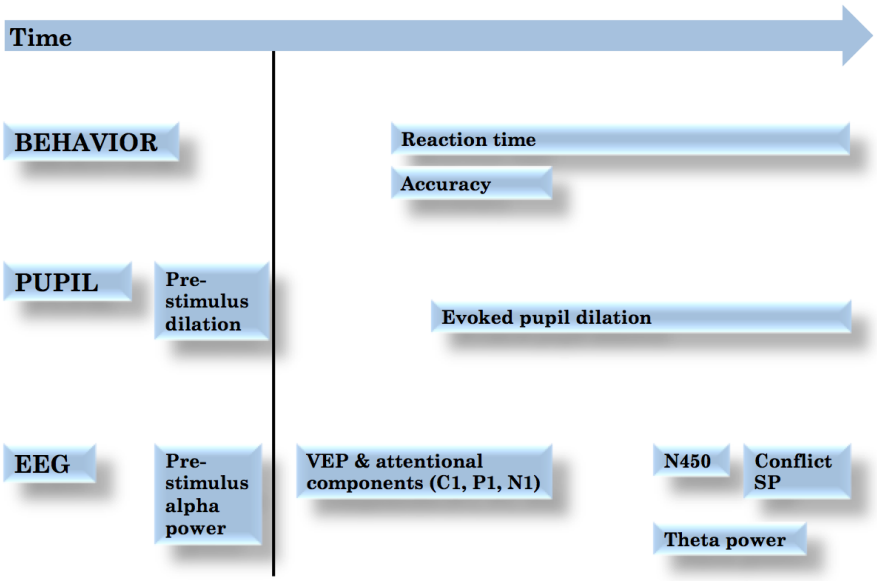

Fig 1. Illustration of possible relationships between measures of behavioral task performance, pupil size measurements and EEG.

Possible future research

Given the lack of studies looking at how psychology-related changes in pupil size affect perception and higher-order cognitive processes, there is still a lot of research that can and should be done. First, it would be interesting to follow-up on our findings and find even better ways to manipulate the size of the pupil. Although we were quite successful in artificially dilating and constricting the size of the pupil, we stuck to a factorial logic in which we compared conditions for which the pupil was large with conditions for which the pupil was small. If it would be possible to decide on the exact size of the pupil beforehand, it would be easier to study the precise underlying optical mechanisms

behind the effects we reported and compare the results with data from previous research. Once could for example try to dilate the pupil with eye drops or use pupil-covering lenses to keep the amount of incoming light constant, although there might be issues related to severe loss of vision or other optical side-effects. Next, independently from the way pupil size is manipulated, researchers could extend the approach to other task domains to get closer to an understanding of the functionality of pupil size changes. An example could be visual search or the ability to detect a simple or complex target feature among a small or large set of distracters (cfr. the feature-integration theory of Treisman & Gelade, 1980). Taking into account that a dilated pupil is associated with decreased visual resolution but increased sensitivity for peripheral stimuli, it can be hypothesized that a large pupil leads to faster target detection times in a search trial with a large set of distracters compared to a small set of distracters (assuming that in a large set, more target stimuli will be presented in the periphery of the visual field). Also the actual location of the target among distracters might be affected by the size of the pupil, since a small pupil will likely be associated with decreased reaction times for finding a target projected on the fovea. Moreover, since we argued that pupil size changes initiated by psychological process most likely still play a functional role, one could even explore if a dilated pupil because of increased mental effort during visual search (Porter, Troscianko, & Gilchrist, 2007) affects the performance on the next trial.

Another example relates to cognitive conflict processing, where, after dilating or constricting the pupil, one could present flanker trials with various distances between the target and distractor arrows. Based on the same sensitivity-acuity trade-off mechanism, it can be expected that participants are more distracted in trials with large distances when

the pupil is large compared to when the pupil is small. Of course, it can be argued that these two examples only study effects of visual deterioration (or loss of vision) and should therefore not be studied by cognitive neuroscientists. However, since the pupil size change stems from a psychological process, we tend to disagree.

CONCLUSION

Taken together, the experiments presented in this dissertation investigated the underlying attentional mechanisms of cognitive control and showed that there is more to pupil size adjustments than previously assumed. We think our main contribution to the field lies in making researchers aware that psychology-related pupil size changes can have a functional role and that future research should take this into account.

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CHAPTER 8:

NEDERLANDSTALIGE SAMENVATTING

Als mensen staan we zelden stil bij de complexiteit van de meest triviale dingen die we doen in het dagelijkse leven. We vinden het normaal dat we wakker worden wanneer de wekker gaat en we zijn niet verrast dat we tegelijkertijd kunnen ontbijten, de krant lezen en emails checken. Cognitieve neurowetenschappers denken wel na over al deze "simpele" vaardigheden en trachten ze op een wetenschappelijke manier te bestuderen. Onderzoek binnen de cognitieve neurowetenschappen focust daarom op de onderliggende mechanismen van zogenaamde "hogere-orde cognitie" en probeert te begrijpen hoe verschillende neurale processen samenwerken om gedrag te bekomen. In deze doctoraatsthesis presenteren we onderzoek naar vroege sensorische aandacht en veranderingen in pupilgrootte die gerelateerd zijn aan cognitieve controle. In de komende paragrafen introduceren we eerst kort de belangrijkste concepten in verband met aandacht, cognitieve controle, pupildilatatie en vroege visuele verwerking. Daarna geven we per hoofdstuk een overzicht van de onderzoeksvragen, de methodes, de resultaten en de interpretatie ervan.

Een van de oudste en meest fundamentele vragen in cognitieve neurowetenschappen gaat over hoe mensen omgaan met de gigantische hoeveelheid informatie die constant wordt opgepikt door de zintuigen. Wanneer je deze dissertatie leest, moet je je volledig concentreren op het boek en tegelijkertijd alles in je omgeving proberen te negeren. Van pop-up venstertjes op je computerscherm tot een bureaugenoot die aan het

telefoneren is, je zal al je aandacht aan het boek moeten wijden. Wanneer dezelfde bureaugenoot echter plotseling je naam vermeldt tijdens zijn telefoongesprek zal je waarschijnlijk opkijken. Dit zogenaamde "*cocktail party effect*" is een goede illustratie van de complexiteit van menselijke aandacht: zelfs wanneer je denkt dat je niet aan het luisteren bent, kan sommige (voor jou belangrijke) informatie doordringen tot het bewustzijn. Er werden verschillende theoretische modellen voor aandacht voorgesteld in het verleden. Het *filter model* van Donald Broadbent (Broadbent, 1958) stelde een filtermechanisme voor dat beslist welke inkomende sensorische signalen verder mogen verwerkt worden. Dit model kon helaas het bovengenoemde cocktail pary effect niet verklaren en werd vervangen door *late-selectie modellen* die voorstelden dat alle simuli non-selectief worden verwerkt (e.g. Deutsch & Deutsch, 1963). Deze modellen konden op hun beurt niet om met de gelimiteerde aandachtscapaciteit en werden vervangen door het *attenuatie model* van Anne Treisman (Treisman, 1964). Dit model stelde voor dat irrelevante stimuli worden geattenueerd (maar niet gefilterd) en dat stimuli geassocieerd met arousal (door semantische betekenis of intensiteit) een lagere drempel zouden hebben om het bewustzijn te bereiken en verder verwerkt te worden.

Pioniers in aandachtsonderzoek onderzochten niet alleen wanneer aandachtsselectie plaatsvindt, maar ook hoe dit precies in zijn werk gaat. Een belangrijk onderscheid kan hierbij gemaakt worden tussen *spatiale aandacht* enerzijds en *feature aandacht* anderzijds (voor een vergelijking, zie Soto & Blanco, 2004). Spatiale aandacht betekent dat de aandacht gericht wordt naar een specifieke locatie in het visuele veld, terwijl feature aandacht inhoudt dat de aandacht gericht is op een

bepaalde niet-spatiale eigenschap van de stimulus (bvb. de kleur). Aandacht wordt vaak onderzocht aan de hand van ERP componenten, die worden bekomen door het gemiddelde EEG signaal te nemen over verschillende trials of "beurten" in een vooraf bepaald tijdsinterval dat de presentatie van de stimulus omvat. Wat betreft spatiale aandacht, hebben zowel de *P1* (posterieure positieve component die ongeveer 100 ms post-stimulus verschijnt) als de *N1* (posterieure negatieve component die ongeveer 150-200 post-stimulus optreedt) een grotere amplitude wanneer de aandacht gericht is op de locatie waar de stimulus verschijnt. Wanneer de aandacht gericht is op een bepaalde eigenschap van een stimulus (zoals kleur of vorm), wordt de *SN* (selection negativity) component geobserveerd tussen 140 en 180 ms na het verschijnen van de stimulus.

Aandacht kan gezien worden als één van de belangrijkste mechanismen achter het meer algemene *cognitieve controle* construct en er wordt zelfs over gedebatteerd of er een verschil is tussen de twee (Cohen, 2017). Desalniettemin kan cognitieve controle worden gedefinieerd als de flexibele en adaptieve regulatie van gedrag in de aanwezigheid van conflicterende stimuli of responses (Cohen, 2017). Wanneer je bijvoorbeeld met je auto rijdt en bij een kruispunt aankomt, moet je stoppen wanneer de verkeerslichten op rood staan. Indien de bestuurder in de wagen voor jou echter doorrijdt, kan je bij onvoldoende aandachtscontrole geneigd zijn hem te volgen. Het is in een dergelijke situatie dus noodzakelijk jouw gedrag aan te passen aan de situatie en automatische of *prepotente* gedragingen te overkomen. Cognitieve controle wordt in het lab typisch onderzocht aan de hand van *controle- of congruentietaken*. In deze congruentietaken moeten proefpersonen

reageren op *taak-relevante informatie* en tegelijke *taak-irrelevante informatie* negeren. In de Stroop taak (Stroop, 1992) bijvoorbeeld, moeten participanten de inktkleur benoemen van woorden die semantisch ook voor een woordkleur staan (bvb., het woord "rood" in groene inkt). Omdat woordlezen de dominante, automatische respons is, gaan proefpersonen trager en minder accuraat antwoorden op incongruente trials (het woord "rood" in groene inkt) dan op congruente trials (het woord "groen" in groene inkt). Het verschil in reactietijd en accuraatheid tussen een congruente en incongruente trial wordt het *congruentie-effect* genoemd.

Onderzoek naar cognitieve controle heeft aangetoond dat het congruentie-effect kan gemoduleerd worden door de congruentie van de vorige trial. Meer bepaald wordt het congruentie-effect kleiner wanneer de voorgaande trial een incongruente trial was dan wanneer de vorige trial een congruente trial was. Dit effect staat ook bekend als het *Gratton effect,* het *conflict-adaptatie effect* of het *congruentie-sequentie effect* (voor reviews, zie Duthoo, Abrahamse, Braem, Boehler, & Notebaert, 2014; Egner, 2007). Het conflict-monitoring model van Botvinick, Braver, Barch, Carter, and Cohen (2001) gaf een theoretische verklaring voor dit effect door te stellen dat wanneer het cognitieve controle systeem conflict detecteert tussen taak-relevante en taak-irrelevante informatie, er meer aandacht wordt besteed aan de taak-relevante informatie. Deze detectie van conflict zou plaatsvinden in de dorsale anterieure cingulate cortex en deze regulatie van aandacht zou worden gestuurd door de dorsolaterale prefrontale cortex (e.g. Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999; Kerns et al., 2004). Wanneer de trial na een incongruente trial incongruent is, zal de

proefpersoon sneller en accurater antwoorden doordat hij de taak-irrelevante informatie beter kan negeren. Wanneer de volgende trial echter congruent is, valt het faciliterende effect van dezelfde informatie in de irrelevante dimensie te hebben weg, waardoor de reactie trager zal zijn en de accuraatheid lager.

Cognitieve controle wordt uiteraard heel sterk beïnvloed door *motivationele factoren* (Krebs & Woldorff, 2017) die zowel intrinsiek (e.g. persoonlijk doel) als extrinsiek (e.g. geld) kunnen zijn (Ryan & Deci, 2000). In het lab wordt vooral de interactie tussen extrinsieke beloning en cognitieve controle onderzocht. Krebs en Woldorff (2017) maakten recentelijk een onderscheid tussen *pre-taak beloningscues* en *stimulus-beloning associaties*. Bij het eerste type is er altijd een cue of stimulus die aangeeft dat een beloning kan verkregen worden op wat volgt. Proefpersonen worden bijvoorbeeld ingelicht dat ze 10 eurocent krijgen bij een correcte en snelle respons op de volgende trial. Bij het tweede type, stimulus-beloning associaties, kan de proefpersoon zich niet voorbereiden en wordt de mogelijkheid tot het verkrijgen van beloning aangegeven door de stimulus zelf. Onderzoek naar beide processen leidde tot de identificatie van een neuraal *beloningssysteem* waarbij het ventrale striatum, mediale midbrain structuren en andere dopaminerge gebieden interageren met de regio's die verantwoordelijk zijn voor een bepaalde taak (Braver, 2015; Schmidt, Lebreton, Cléry-Melin, Daunizeau, & Pessiglione, 2012).

Een interessante bevinding in het onderzoek naar cognitieve controle was dat incongruente trials geassocieerd zijn met *gedilateerde pupillen* (Brown et al., 1999; Laeng & Endestad, 2012; Siegle, Ichikawa,

& Steinhauer, 2008; Steinhauer, Siegle, Condray, & Pless, 2004). Deze gedilateerde pupil reflecteert waarschijnlijk de mentale inspanning en arousal die gepaard gaat met de verhoogde aandachtscontrole bij incongruente trials (Siegle et al., 2008). Het gebruik van de pupil als indirecte meting van latente hersenprocessen zoals aandacht of controle is niet nieuw, sinds Hess en Pold al in de jaren '60 aantoonden dat de pupil niet enkel reageert op veranderingen in omgevingslicht (i.e. automatische lichtreflex van de pupil), maar ook op de emotionele valentie van een afbeelding. Deze bevinding leidde tot een exponentiële toename van studies die pupilgrootte rapporteerden als proxy van cognitieve activiteit. De meeste cognitie-gerelateerde veranderingen in pupilgrootte kunnen verklaard worden door de hoge temporele samenhang met activiteit in het locus coeruleus-norepinephrine systeem (LC-NE systeem; Costa & Rudebeck, 2016; Joshi, Li, Kalwani, & Gold, 2016). Dit systeem bestaat uit een subcorticale locus coeruleus (LC) die norepineprhine (NE) verspreidt in het brein, wat een belangrijke rol speelt bij aandachtsregulatie.

Nu we meest belangrijke concepten kort geïntroduceerd hebben waardoor het onderzoek in deze dissertatie beter gekaderd kan worden (voor een meer uitgebreide introductie verwijzen we graag naar hoofdstuk 1), is het tijd om de specifieke onderzoeksvragen te presenteren die we in deze doctoraatsthesis gesteld hebben en de belangrijkste bevindingen en conclusie toe te lichten. In de grijze kaders presenteren we de belangrijkste bevinding uit elk hoofdstuk, gevolgd door een meer gedetailleerde uitleg.

"Een adaptief mechanisme gebaseerd op relatieve spatiale inhibitie is een onderliggend mechanisme van het conflict adaptatie effect in een context van temporele voorspelbaarheid."

In hoofdstuk 2 ligt de focus op de onderliggende aandachtsmechanismen van het conflict adaptatie effect. Zoals hierboven uitgelegd, voorspellen cognitieve controle theorieën zoals de conflict monitoring theorie verhoogde aandachtsallocatie na incongruente trials, die op hun beurt het congruentie-effect verkleinen. Voorgaand onderzoek heeft voornamelijk fMRI gebruikt om deze mechanismen te bestuderen, maar deze methode heeft helaas een zeer lage temporele resolutie en kan moeilijk discrimeren tussen toegenomen aandacht voor taakrelevante informatie en verminderde aandacht voor taakirrelevante informatie. Daarom kozen we ervoor om het op EEG gebaseerde paradigma van Appelbaum, Boehler, Won, Davis, en Woldorff (2012) te gebruiken waarbij de taakirrelevante informatie (i.e. het kleurwoord in de Stroop taak) 200 ms voor, op hetzelfde moment, of na de presentatie van de taakrelevante inktkleur werd gepresenteerd. Het idee was dat dit tijdsvenster van 200 ms ons zou toelaten om de aandachtsallocatie voor de relevante en irrelevante informatie afzonderlijk te kunnen bekijken en beter het effect na te kunnen gaan van de voorgaande congruentie. We begonnen met twee Stroop experimenten, maar breidden achteraf onze benadering uit naar de Flanker taak. Waar Stroop conflict zowel spatiale als non-spatiale aandacht meet, gaat Flanker conflict voornamelijk spatiale aandacht meten (Luck & Kappenman, 2012). Voor elk type conflict hadden we één experiment waarbij de irrelevante informatie random gepresenteerd

werd voor, na of op hetzelfde moment als de relevante dimensie en één experiment waarbij de irrelevante informatie altijd voor de relevante kwam. Onze hypothese was dat na een incongruente trial minder aandacht zou worden toebedeeld aan de irrelevante informatie wanneer deze gepresenteerd werd kort voor de relevante, terwijl er meer aandacht zou worden gegeven wanneer de relevante voor de irrelevante zou komen, sinds voorgaand fMRI onderzoek evidentie had getoond voor beide mechanismen (Egner & Hirsch, 2005; King, Korb, von Cramon, & Ullsperger, 2010; Polk, Drake, Jonides, Smith, & Smith, 2008). We vonden evidentie voor deze hypothese in een van de vier experimenten, namelijk in het Flanker experiment waarbij proefpersonen konden voorspellen dat in de volgende trial irrelevante informatie eerst zou worden gepresenteerd. Ongeveer 150 ms na de presentatie van de distracter observeerden we een aandachtsgerelateerde N1 component die een kleinere amplitude had na incongruente trials dan na congruente trials. Deze modulatie ging gepaard met een modulatie van inter-trial mid-frontale thetha power en een theta-power conflict adaptatie effect. Daarnaast was er in deze specifieke conditie ook een significant conflict adaptatie effect in de gedragsdata. We interpreteerden deze resultaten als evidentie voor een adaptief mechanisme gebaseerd op relatieve aandachtsinhibitie na de ervaring van cognitief conflict. Het feit dat deze modulatie niet werd gevonden in trials waarbij de relevante dimensie eerst of op hetzelfde moment werd aangeboden, kwam waarschijnlijk door dat proefpersonen te weinig conflict ervaarden bij deze trials (i.e. ze waren te gemakkelijk voor de proefpersoon). Wanneer er weinig conflict wordt gedetecteerd, zal het controlesysteem uiteraard minder de neiging hebben controle bij te

sturen. Daarnaast kan het feit dat de modulatie enkel werd gevonden in de Flanker taak te maken hebben met het type aandacht. De Stroop taak meet voornamelijk feature aandacht, terwijl de Flanker taak ook spatiale aandacht meet. Het kan dus zijn dat onze modulatie een spatiaal aandachtsmechanisme reflecteert (na conflict wordt er minder aandacht toebedeeld aan het linker- en rechter visueel veld waar de distracters zich bevinden). Ten slotte denken we dat de modulatie enkel optrad in de voorspelbare context omdat het om een proactief controle mechanisme gaat. Wanneer de proefpersoon niet kan inschatten of de volgende trial met taak-irrelevante of taak-relevante informatie begint (onvoorspelbare context), zou het een nadeel zijn om een automatische aandachtsfilter te hanteren, alhoewel dat net hetgene is wat op basis van reactive controle kan verwacht worden.

Samengevat kunnen we dus stellen dat we een klein stukje van de puzzel oplossen door één bepaald mechanisme van aandachtsregulatie tijdens het conflict adaptatie effect uit te klaren. Verder onderzoek is nodig om duidelijkheid te scheppen over meer algemene mechanismen.

" Pupilgrootte heeft een direct effect op V1: een grote pupil leidt tot verminderde activatie"

Alhoewel hoofdstuk 3 inhoudelijk niet rechtstreeks verder bouwt op bevindingen in hoofdstuk 2, was het er wel door geïnspireerd. Laeng, Orbo, Holmlund, and Miozzo (2011) stelden vast dat de verhoogde mentale inspanning tijdens incongruente trials de grootte van de pupil deed toenemen. We redeneerden dat het daarom niet ondenkbaar is dat pupilgrootte ook een rol speelt in een proces als conflict adaptatie,

waarbij de gedilateerde pupil in trial n-1 een effect heeft op trial n. Maar vooraleer naar hogere-orde of psychologische processen te kijken, besloten we te beginnen met het effect van pupilgrootte op zogenaamde "low-level" visuele processen te onderzoeken. De primaire visuele cortex (V1) die zich in de posterieure occipitale lob bevindt, is het eerste stadium van corticale visuele verwerking en wordt in het EEG gereflecteerd door de C1 component. Deze C1 component is een positieve of negatieve ERP component (afhankelijk van de positie van de stimulus in het visuele veld) die tussen de 50 en 100 ms na de presentatie van een visuele stimulus verschijnt.

In een eerste experiment maakten we gebruik van de procedure van Binda, Pereverzeva, and Murray (2013) om de grootte van de pupil artificeel klein of groot te maken. Proefpersonen moesten coverte aandacht geven aan een witte of zwarte cirkel die links en rechts van het fixatiepunt werden gepresenteerd. Bij coverte aandacht blijft de proefpersonen het fixatiepunt fixeren, waardoor de fysieke stimulatie van de stimuli exact hetzelfde was. Door deze procedure werd de pupil groot wanneer proefpersonen naar de zwarte cirkel staarden en klein wanneer ze naar de witte cirkel keken. 1800, 2200 en 2600 ms nadat de cirkels verschenen, werd een C1-opwekkende stimulus gepresenteerd die bestond uit een groot aantal korte, witte, horizontale lijntjes op een zwarte achtergrond. Op een subset van trials moesten proefpersonen een kleurswijziging van blauw naar geel in het middelpunt van een cirkel detecteren, wat ons toeliet na te gaan of proefpersonen de taak correct uitvoerden of niet. In een tweede experiment manipuleerden we de grootte van de pupil aan de hand van een paradigma van Laeng and Endestad (2012). Proefpersonen fixeerden twee verschillende visuele

illusies die uit exact dezelfde elementen bestonden (en dus niet verschilden in fysieke stimulatie). De ene illusie gaf de impressie weinig licht uit te stralen (grote pupil), terwijl de andere illusie als heel helder werd gepercipieerd (kleine pupil). Opnieuw presenteerden we een C1-opwekkende stimulus na een bepaald interval.

De resultaten van beide experimenten gaven aan dat de amplitudegrootte van de C1 component kleiner was wanneer de pupil groot was vergeleken met wanneer de pupil klein was. Er was geen significant verschil in prestatie op de catch trials in experiment 1, wat aangaf dat mensen evenveel mentale inspanning leverden in beide condities. We interpreteerden dit effect van pupilgrootte op de C1 component volgens de zogenaamde sensitivity-acuity trade-off (Loewenfeld & Lowenstein, 1999). Deze trade-off verwijst naar het feit dat meer of minder licht op de retina een inverse relatie inhoudt tussen visuele resolutie (iets in detail kunnen zien) en visuale sensitiviteit (de aanwezigheid van een vage stimulus in de visuele periferie kunnen detecteren). Als er veel licht is en de pupil vernauwt, zal het beeld op de retina scherper zijn doordat lichtstralen die van verschillende dieptes komen minder gebroken worden en dus op een kleiner gebied op de retina worden geprojecteerd. Deze verhoogde visuele resolutie gaat verloren bij weinig licht waarbij de pupil moet vergroten en er dus een groter gebied van de retina wordt geactiveerd (wazig beeld). Aangezien het detecteren van contrasten in luminatie (bvb. de scheiding tussen een wit en zwart vlak) grotendeels in V1 plaatsvindt en we gebruik hebben gemaakt van C1-opwekkende stimuli met een hoge spatiale frequentie, is een verlaagde visuele resolutie inderdaad een plausibele verklaring voor het effect dat we observeerden.

" Het is onwaarschijnlijk dat het effect van pupilgrootte op activiteit in V1 verklaard kan worden door aandacht of mentale inspanning"

Hoofdstuk 4 was een rechtstreekse vervolgstudie op de experimenten beschreven in experiment 3. Aangezien het effect van pupilgrootte op de C1 respons belangrijke implicaties heeft voor een groot aantal studies die pupildilatatie hebben gemeten, wouden we dit effect repliceren en eventuele alternatieve verklaringen uitsluiten. Alternatieve verklaringen hebben vooral te maken met de manier waarop we de pupil artificieel kleiner en groter hebben gemaakt in experiment 1 van hoofdstuk 3: aangezien proefpersonen steeds het middelpunt fixeerden, was er geen verschil in fysieke stimulatie (i.e. de luminantie was exact gelijk) mogelijk, maar men kan nog steeds argumenteren dat het indirect aandacht geven aan een zwarte of witte cirkel tot een bepaalde "cognitieve staat" kan leiden die de C1 component beïnvloedt. Deze alternatieve verklaring geldt niet voor experiment 2 in hoofdstuk 3, aangezien proefpersonen daar steeds dezelfde figuur (in een andere configuratie) centraal fixeerden.

In een nieuw experiment maakten we gebruik van de relatief trage respons van de pupil om een C1-uitlokkende stimulus te presenteren voor en na de pupil een verschil vertoonde (T1: 400 ms na de presentatie van de cirkels; T2: 2200 ms na de presentatie van de cirkels). Daarnaast waren we geïnteresseerd in alpha-power lateralisatie als een index van aandachtsallocatie. Alpha power daalt bij verhoogde aandacht, wat het interessant maakt om na te gaan of er een verschil was tussen de condities. Net zoals in het vorige hoofdstuk waren er ook catch trials om gedragsmatig na te gaan of proefpersoon

dezelfde inspanning leverden in de verschillende condities. De resultaten toonden aan dat het effect van pupilgrootte op de C1 component kon gerepliceerd worden voor de T2 trials (de trials waarbij er een verschillende pupilgrootte was). Opnieuw resulteerde een grotere pupil in een kleinere amplitude. Voor T1 trials vonden we geen verschil in C1-amplitude, wat in de lijn van onze verwachtingen lag. Wat betreft de alpha-power lateralisatie konden we aantonen dat proefpersonen reeds hun aandacht hadden verlegd naar de linker-of rechterkant op het moment van T1 presentatie. Dit toonde aan dat de alternatieve verklaring voor het pupileffect via een aandachtsafhankelijke "cognitieve staat" kon verworpen worden, aangezien we geen verschil vonden bij T1.

" Toegenomen aandacht en een langdurige toename in pupilgrootte is geen garantie voor een beter prestatie in een belonende context"

In hoofstuk 5 onderzochten we de relatie tussen aandacht, cogntitieve controle en pupildilatatie door middel van een gecombineerd EEG-eyetracking experiment. Meer bepaald waren we geïnteresseerd in langdurige effecten van beloning op de onderliggende aandachtsmechanismen van cognitieve controle. Het is immers aangetoond dat langdurige beloningseffecten de taakprestatie ten voordele komen en tot verhoogde activiteit in controle-gerelateerde pre-frontale hersengebieden leiden (e.g. Jimura, Locke, & Braver, 2010). In ons experiment wouden we deze bevindingen uitbreiden naar een typische controletaak zoals de Eriksen Flanker taak en gedragsmatige en elektrofysiologische markers van aandacht (P1 en N1 componenten)

met beloningsgerelateerde verschillen in pupilgrootte in verband brengen. Dit verband kan verwacht worden op basis van voorgaand onderzoek, aangezien vele onderzoekers een nauwe koppeling hebben vastgesteld tussen pupildilatatie en het aandachtsmodulerende LC-NE systeem (Aston-Jones & Cohen, 2005; Aston-Jones, Rajkowski, Kubiak, & Alexinsky, 1994; Eckstein, Guerra-Carrillo, Miller Singley, & Bunge, 2016; Gilzenrat, Nieuwenhuis, Jepma, & Cohen, 2010; Rajkowski, Kubiak, & Aston-Jones, 1994). Net zoals in hoofdstuk 2 wouden we gebruik maken van de hoge temporele resolutie van EEG en kunnen discrimeren tussen de relevante en irrelevante stimulusdimensies (Appelbaum et al., 2012). We lieten proefpersonen een Flanker taak uitvoeren met 4 responsmogelijkheden waarbij ze geldbeloningen kregen voor snelle en accurate responsen in 2 van 4 blokken. Om te zorgen dat het congruentie-effect groot genoeg was om verschillen tussen belonende en niet-belonende blokken te kunnen vinden, presenteerden we de irrelevante dimensie steeds 200 ms voor de relevante dimensie. Onze hypothese was dat in een belonende context, minder aandacht zou worden toebedeeld aan de distracter pijlen en dat dit zou worden gereflecteerd in een kleinere aandachtsgerelateerde N1 component (gerelateerd aan de distracter verwerking). Daarentegen verwachtten we een grotere N1 component gerelateerd aan de target. Met betrekking tot pupildilatatie verwachtten we dat een belonende context zou geassocieerd zijn met een langdurige toename in baseline pupilgrootte (i.e. duur van het blok). Daarenboven wouden we nagaan of het verschil in pupilgrootte tussen de belonende en niet-belonende blokken een marker zou kunnen zijn van de hoeveelheid mentale inspanning of aandachtsallocatie proefpersonen investeerden en of dit

verschil de grootte van de N1 component zou kunnen voorspellen.

In tegenstelling tot onze verwachtingen waren we niet in staat de typische beloningseffecten terug te vinden die normaal worden vastgesteld in experimenten met belonende blokken (Chiew & Braver, 2014; Jimura et al., 2010; Langford, Krebs, Talsma, Woldorff, & Boehler, 2016; Massar, Lim, Sasmita, & Chee, 2016; Paschke et al., 2015; Schevernels et al., 2015; Small et al., 2005; Soutschek, Stelzel, Paschke, Walter, & Schubert, 2015; Soutschek, Strobach, & Schubert, 2014). We vonden echter wel een significant verschil in de posterieure negatieve ERP component van 150 tot 200 ms na de presentatie van de distracter (dus voor de target pijl werd gepresenteerd), die we eerst identificeerden als de aandachtsgerelateerde N1 component door zijn timing en topografie. Deze negatieve component was echt meer uitgesproken bij midline electrodes dan bij gelateraliseerde electrodes, wat het mogelijk maakt dat onze bevinding een meer algemeen sensorisch "gating" mechanisme reflecteert waarbij een toename in aandachtsallocatie tot een boost in de signal-to-noise ratio leidt. Deze bevinding was dus ook tegengesteld aan onze verwachtingen, aangezien we een beloningsgerelateerde strategische inhibitie van distracter verwerking hadden verwacht. Daarboven observeerden we geen toename in aandachtsallocatie voor de target pijlen, maar dit kan te wijten zijn aan de overlap in het EEG signaal door de respons op de distracter verwerking.

Kortom, we denken dat deze bevindingen evidentie bieden voor het feit dat een belonende context tot een langdurige toename in aandacht zorgt en geen ruimte laat voor strategische inhibitie, ook al levert dit niet altijd een voordeel voor de taakprestatie op. Dit is ook in

lijn met onderzoek van Schevernels et al. (2015), die hetzelfde observeerde in belonende stop-signaal taak.

" Variaties in pupilgrootte die gedreven zijn door psychologische processen kunnen een functionele rol spelen door de balans tussen visuele resolutie en perifere sensitiviteit te wijzigen"

Het onderzoek beschreven in hoofdstukken 3 en 4 toont aan dat pupilgrootte een effect kan hebben op vroege visuele processen in de visuele cortex. Dit inspireerde ons om een opinie/review paper te schrijven over de vaak genegeerde functionele rol van pupilgrootte in studies die licht-onafhankelijke veranderingen in pupilgrootte gebruiken als indirecte marker van interne psychologische processen zoals aandacht, mentale inspanning en arousal. De motivatie om pupilgrootte te meten heeft te maken met het feit dat het tot inzichten kan leiden in psychologische processen die niet onmiddelijk duidelijk kunnen zijn in gedragsdata of die anders heel moeilijk te operationaliseren zijn (zoals bvb. cognitieve inspanning). Wij vonden het echter opvallend dat pupilgrootte enkel beschouwd wordt als een indirecte marker, en ervan uitgegaan wordt dat de verandering in grootte zelf functioneel irrelevant is en een enkel een "uitkomst" van een ander proces betreft. Daarom beargumenteren we dat veranderingen in pupilgrootte, gedreven door psychologische processen, wel een functionele rol kunnen hebben door het te relateren aan de hierboven vermelde sensitivity-acuity trade-off. Verder onderzoek is echter nodig om uit te klaren bij welke psychologische processen het functioneel is dat de visuele resolutie verhoogt (door een constrictie van

de pupil) en bij welke processen het functioneel is dat de sensitiviteit voor perifere stimuli verhoogt (door een dilatatie van de pupil).

Samenvattend, de experimenten die we in deze dissertatie hebben gepresenteerd onderzochten de onderliggende aandachtsmechanismen van cognitieve controle en toonden aan dat wijzigingen in pupilgrootte meer kunnen betekenen dan vooralsnog werd aangenomen. Psychologie-gerelateerde veranderingen in pupilgrootte hebben waarschijnlijk een functionele rol en we denken dat toekomstig onderzoek hier steeds rekening mee zou moeten houden.

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DATA STORAGE FACT SHEETS

In compliance with the UGent standard for research accountability, transparacy and reproducibility, the location of the datasets used in this dissertation are added below. For each of the empirical chapters (i.e., chapters 2 to 5) a separate Data Storage Fact Sheet is completed, detailing which data and analysis files are stored, where they are stored, who has access to the files and who can be contacted in order to request access to the files. In addition, the Data Storage Fact Sheets have been added to my public UGent Biblio account.

DATA STORAGE FACT SHEET FOR CHAPTER 2

% Data Storage Fact Sheet

% Name/identifier study
% Author: Klaas Bombeke
% Date: 01-06-2017

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- address: Henri Dunantlaan 2 9000 Gent

- e-mail: Nico.boehler@ugent.be

If a response is not received when using the above contact details, please send an email to data.pp@ugent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium.

2. Information about the datasets to which this sheet applies
==========
* Reference of the publication in which the datasets are reported:

Bombeke, K., Langford, Z. D., Notebaert, W., & Boehler, C. N. (2017). The role of temporal predictability for early attentional adjustments after conflict. PlosOne, 12(4).

* Which datasets in that publication does this sheet apply to?:

Dataset for experiment 1,2,3 and 4

3. Information about the files that have been stored
==========

3a. Raw data
---

* Have the raw data been stored by the main researcher? [x] YES / [ ] NO
If NO, please justify:

* On which platform are the raw data stored?
- [x] researcher PC
- [ ] research group file server
- [x] other (specify): External hard drive owned by the lab

* Who has direct access to the raw data (i.e., without intervention of another person)?
- [x] main researcher
- [x] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

3b. Other files
---

* Which other files have been stored?
 - [] file(s) describing the transition from raw data to reported results. Specify:
 - [x] file(s) containing processed data. Specify: following each step in the data processing a new version of the datafile was stored. The data was also saved for RT analysis and accuracy analysis separately.
 - [x] file(s) containing analyses. Specify: SPPS and Matlab scripts for the analysis
 - [x] files(s) containing information about informed consent
 - [ ] a file specifying legal and ethical provisions
 - [ ] file(s) that describe the content of the stored files and how this content should be interpreted. Specify: ...
 - [ ] other files. Specify: ...

* On which platform are these other files stored?
 - [x] individual PC
 - [ ] research group file server
 - [x] other: External hard drive owned by the lab

* Who has direct access to these other files (i.e., without intervention of another person)?
 - [x] main researcher
 - [x] responsible ZAP
 - [ ] all members of the research group
 - [ ] all members of UGent
 - [ ] other (specify): ...

4. Reproduction
===

* Have the results been reproduced independently?: [ ] YES / [x] NO

* If yes, by whom (add if multiple):
  - name:
  - address:
  - affiliation:
  - e-mail:

DATA STORAGE FACT SHEET FOR CHAPTER 3

% Data Storage Fact Sheet

% Name/identifier study
% Author: Klaas Bombeke
% Date: 01-06-2017

1. Contact details
==========

1a. Main researcher

- name: Klaas Bombeke
- address: Henri Dunantlaan 2 9000 Gent
- e-mail: bombeke.klaas@gmail.com

1b. Responsible Staff Member (ZAP)

- name: Nico Boehler
- address: Henri Dunantlaan 2 9000 Gent
- e-mail: Nico.boehler@ugent.be

If a response is not received when using the above contact details, please send an email to data.pp@ugent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium.

2. Information about the datasets to which this sheet applies
==========
* Reference of the publication in which the datasets are reported:

Bombeke, K., Duthoo, W., Mueller, S., Hopf, J-.M., & Boehler, C. N. (2016). Pupil size directly modulates the feedforward response in human primary visual cortex independently of attention. Neuroimage, 127, 67-73.

* Which datasets in that publication does this sheet apply to?:

Dataset for experiment 1 and 2

3. Information about the files that have been stored
==========

3a. Raw data
----

* Have the raw data been stored by the main researcher? [x] YES / [ ] NO
If NO, please justify:

* On which platform are the raw data stored?
 - [x] researcher PC
 - [ ] research group file server
 - [x] other (specify): External hard drive owned by the lab

* Who has direct access to the raw data (i.e., without intervention of another person)?
 - [x] main researcher
 - [x] responsible ZAP
 - [ ] all members of the research group
 - [ ] all members of UGent
 - [ ] other (specify): ...

3b. Other files
----

* Which other files have been stored?
 - [] file(s) describing the transition from raw data to reported results. Specify:
 - [x] file(s) containing processed data. Specify: following each step in the data processing a new version of the datafile was stored. The data was also saved for RT analysis and accuracy analysis separately.
 - [x] file(s) containing analyses. Specify: SPPS and Matlab scripts for the analysis
 - [x] files(s) containing information about informed consent
 - [ ] a file specifying legal and ethical provisions
 - [ ] file(s) that describe the content of the stored files and how this content should be interpreted. Specify: ...
 - [ ] other files. Specify: ...

* On which platform are these other files stored?

- [x] individual PC
- [ ] research group file server
- [x] other: External hard drive owned by the lab

* Who has direct access to these other files (i.e., without intervention of another person)?
- [x] main researcher
- [x] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

4. Reproduction
==========
* Have the results been reproduced independently?: [ ] YES / [x] NO

* If yes, by whom (add if multiple):
- name:
- address:
- affiliation:
- e-mail:

DATA STORAGE FACT SHEET FOR CHAPTER 4

% Data Storage Fact Sheet

% Name/identifier study
% Author: Klaas Bombeke
% Date: 01-06-2017

1. Contact details
==========

1a. Main researcher

- name: Klaas Bombeke
- address: Henri Dunantlaan 2 9000 Gent
- e-mail: bombeke.klaas@gmail.com

1b. Responsible Staff Member (ZAP)

- name: Nico Boehler
- address: Henri Dunantlaan 2 9000 Gent
- e-mail: Nico.boehler@ugent.be

If a response is not received when using the above contact details, please send an email to data.pp@ugent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium.

2. Information about the datasets to which this sheet applies
==========
* Reference of the publication in which the datasets are reported:

Bombeke, K., Hopf, J-.M., & Boehler, C. N. (under review). Revisiting the influence of the pupil on feedforward primary visual cortex actvity: discriminating effects of attentional state and pupil size. *Psychophysiology*.

* Which datasets in that publication does this sheet apply to?:

Dataset for experiment 1

3. Information about the files that have been stored
==========

3a. Raw data
---

* Have the raw data been stored by the main researcher? [x] YES / [ ] NO
If NO, please justify:

* On which platform are the raw data stored?
 - [x] researcher PC
 - [ ] research group file server
 - [x] other (specify): External hard drive owned by the lab

* Who has direct access to the raw data (i.e., without intervention of another person)?
 - [x] main researcher
 - [x] responsible ZAP

- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

3b. Other files
---

* Which other files have been stored?
- [] file(s) describing the transition from raw data to reported results. Specify:
- [x] file(s) containing processed data. Specify: following each step in the data processing a new version of the datafile was stored. The data was also saved for RT analysis and accuracy analysis separately.
- [x] file(s) containing analyses. Specify: SPPS and Matlab scripts for the analysis
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- [x] other: External hard drive owned by the lab

* Who has direct access to these other files (i.e., without intervention of another person)?
- [x] main researcher
- [x] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

4. Reproduction
==========
* Have the results been reproduced independently?: [ ] YES / [x] NO

* If yes, by whom (add if multiple):
- name:
- address:
- affiliation:

- e-mail:

DATA STORAGE FACT SHEET FOR CHAPTER 5

% Data Storage Fact Sheet

% Name/identifier study
% Author: Klaas Bombeke
% Date: 01-06-2017

1. Contact details
==========

1a. Main researcher

- name: Klaas Bombeke
- address: Henri Dunantlaan 2 9000 Gent
- e-mail: bombeke.klaas@gmail.com

1b. Responsible Staff Member (ZAP)

- name: Nico Boehler
- address: Henri Dunantlaan 2 9000 Gent
- e-mail: Nico.boehler@ugent.be

If a response is not received when using the above contact details, please send an email to data.pp@ugent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium.

2. Information about the datasets to which this sheet applies
==========
* Reference of the publication in which the datasets are reported:

Bombeke, K., Kostandyan, M., Notebaert, W., & Boehler, C. N. Increased effort without behavioral pay-off: Sustained pupil dilation and increased attentional processing in a rewarded context. *Manuscript in preparation*

* Which datasets in that publication does this sheet apply to?:

Dataset for experiment 1

3. Information about the files that have been stored
==========

3a. Raw data
---

* Have the raw data been stored by the main researcher? [x] YES / [ ] NO
If NO, please justify:

* On which platform are the raw data stored?
 - [x] researcher PC
 - [ ] research group file server
 - [x] other (specify): External hard drive owned by the lab

* Who has direct access to the raw data (i.e., without intervention of another person)?
 - [x] main researcher
 - [x] responsible ZAP
 - [ ] all members of the research group
 - [ ] all members of UGent
 - [ ] other (specify): ...

3b. Other files
---

* Which other files have been stored?
 - [] file(s) describing the transition from raw data to reported results. Specify:
 - [x] file(s) containing processed data. Specify: following each step in the data processing a new version of the datafile was stored. The data was also saved for RT analysis and accuracy analysis separately.
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 - [x] responsible ZAP
 - [ ] all members of the research group
 - [ ] all members of UGent
 - [ ] other (specify): ...

4. Reproduction
==========
* Have the results been reproduced independently?: [ ] YES / [x] NO

* If yes, by whom (add if multiple):
  - name:
  - address:
  - affiliation:
  - e-mail: